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The Effects of Early Life Exposures on Health Outcomes Throughout the Life Course

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The Effects of Early Life Exposures on Health Outcomes Throughout the Life Course

by

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Dedication

Dedicated to my parents and brother for their infinite love, support and advice over the years; to my friends, who picked me up during the hard times and shared the joy during the good times; and to my mentor, Dr. Forman, for showing me the threads of nutritional epidemiology from the eyes of a true expert and for always having my back.

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Abstract

The Effects of Early Life Exposures on Health Outcomes Throughout the Life Course

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Obesity is on the rise worldwide. The goal of this research is to examine the effects of important early life exposures, notably age at solid food introduction during infancy, and television viewing and physical activity during childhood, on obesity across the life course. Chapter 1 summarizes prior research on these exposures in relation to incidence of obesity and changes in anthropometric trajectories over time. The gaps in the literature that led to development of these aims are also described in this chapter. Chapter 2 describes results of an analysis of the association between age at solid food introduction, an important turning point in infant feeding practices, and obesity throughout life. Late age at solid food introduction (≥9 months versus 6-9 months) was associated with marginally higher odds of obesity at age five among girls, but this association did not persist at later ages. Chapter 3 discusses research on the effects of television viewing in childhood alone, and in combination with physical activity, on overweight and obesity in childhood, adolescence and adulthood. Compared to girls who watched no television at 3-5 and 5-10 years, girls who watched television for four or more hours per day had higher odds of obesity throughout the life course. The joint effects of long hours of television viewing and low physical activity during childhood

resulted in higher odds of obesity that persisted from childhood to adulthood. Chapter 4 describes the association between childhood television viewing and change in body mass index and weight Z-scores from childhood through adolescence, and waist circumference and waist-to-height ratio Z-scores in adolescence in a Norwegian population. Children who watched ≥2 hours of television/day, versus ≤0.5 hours/day, had a higher body mass index Z-score trajectory from childhood to adolescence, but not weight Z-score trajectory, or waist circumference and waist-to-height ratio Z-scores in adolescence. Finally, these findings are summarized, their public health implications are discussed and future directions are indicated in Chapter 5.

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Chapter 1: Introduction

LIFE COURSE EPIDEMIOLOGY: HISTORY AND BIOLOGY

The focus of epidemiologists over the past century has shifted from communicable illnesses and diseases of nutrient deficiencies to non-communicable conditions, such as obesity, type 2 diabetes and cardiovascular disease. Initially, these conditions were explored in association with proximal lifestyle and dietary risk factors.[1] Over the past few decades, research efforts turned to the independent, interactive and cumulative effects of exposures across an individual's life course to explain the etiology of major diseases with global epidemics – i.e. taking a life course approach to chronic disease epidemiology.[2]

Life course epidemiology rests on the notion that, adult chronic diseases are ultimately the result of behavioral, biological, social and psychological exposures interacting and accumulating at critical windows across an individual's life course (Figure 1.1).[3,4] Identification of risk factors earlier in life may result in more effective interventions at target periods to reduce risk of disease later in life. A life course approach does not negate the possibility of later-life intervention, but rather emphasizes time (latency period before clinical disease manifests) and timing (life stage at which exposure occurs) in understanding disease etiology.[5] Life course epidemiology links the perinatal, adolescent and adult life periods with a focus on preclinical endpoints, biomarkers of disease, clinical disease endpoints and/or trajectories of phenotypes across life.[5] A life course approach to health and disease forms the primary basis of the following chapters, which focus on exposures during infancy and childhood, and risk of obesity across the life course.

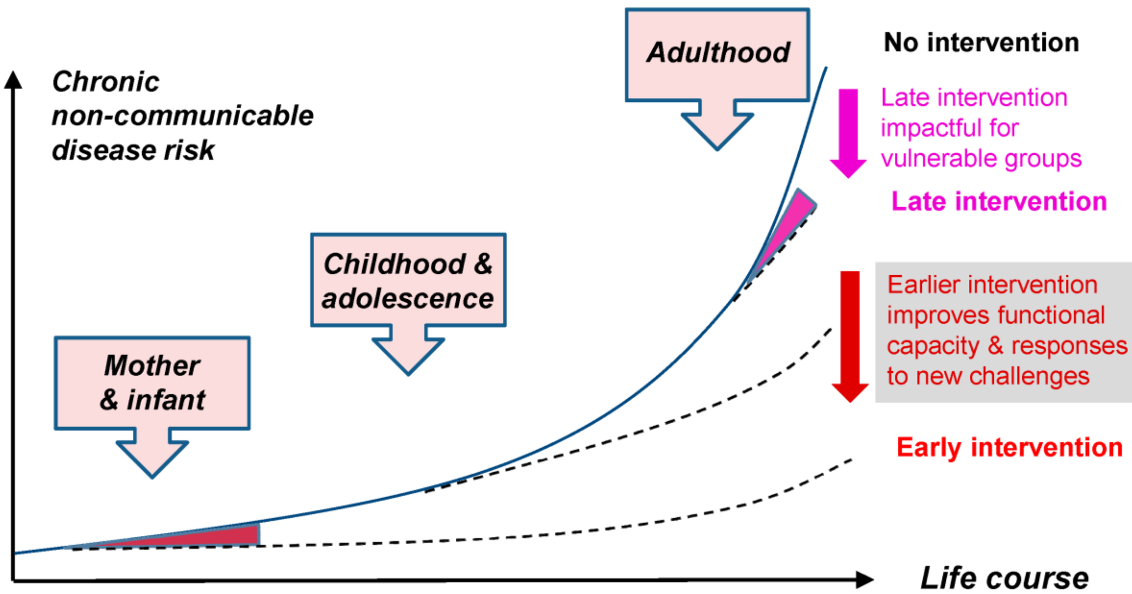


Figure 1.1: A Life Course Approach to Health and Disease[3]

OBESITY: A LIFE COURSE APPROACH

The obesity epidemic in the United States affects 17% of children, 21% of adolescents and 38% of adults, making it one of the most serious health issues plaguing the nation today.[6,7] Although these rates have not dramatically changed since the 2003-2004 National Health and Nutrition Examination Survey (NHANES), the numbers remain alarmingly high and warrant attention.[8] Large prospective cohort studies have shown that childhood body mass index (BMI) is positively correlated with adult BMI,[9] and that childhood obesity is associated with adult adiposity.[10] Additionally, both childhood and adult obesity are associated with an array of metabolic co-morbidities, bone and joint issues, reduced life expectancy and poor psychological state.[11]

Obesity is a multifactorial condition with complex modifiable and non-modifiable drivers acting at different points on the continuum from early life to late adulthood.[12] Although excessive caloric intake coupled with a sedentary lifestyle have been the primary culprits,[13] other risk factors have emerged which may act synergistically or independently across the life course to influence risk of obesity.

Maternal obesity,[14] smoking,[15] gestational weight gain[14] and diabetes,[16] as well as exposure to famine[17] and endocrine-disrupting chemicals[18] have been implicated in the index offspring's risk of obesity. These exposures likely act through epigenetic fetal programming. Infant feeding practices, such as the duration and exclusivity of breastfeeding versus formula feeding,[19] the age at which solid foods are introduced[20] and early life diet[21] may also impact obesity. Furthermore, screen time and other sedentary behaviors during childhood and adolescence,[22,23] coupled with biological changes such as adiposity rebound[24] and puberty[25] could also contribute to development of obesity. Other factors acting throughout life include income, education, sleep and the built environment.[12] The combination of these risk factors exert their influence at different stages of growth and development, and interact with genes to ultimately determine risk of obesity throughout the life course.

Amidst a plethora of research on risk factors for obesity, there is much to gain from large, prospective cohort studies linking early modifiable behaviors to obesity across the life course. As such, the following chapters focus on three modifiable risk factors potentially related to obesity: age at solid food (SF) introduction during infancy; and television viewing (TV) and physical activity (PA) during early and late childhood.

AGE AT SOLID FOOD INTRODUCTION

Over the past few decades, complementary feeding recommendations have changed considerably. In a review of infant feeding trends prior to the 1920's, infants were introduced to SF at one year of age, while in the 1930s-1960s, baby food (beikost) was introduced to infants from as early as two days of age.[26,27] Age at SF introduction covaried by birth cohorts, similar to variation in breastfeeding rates from the Great Depression up to the Baby Boom generation.[28]

Currently, the American Academy of Pediatrics recommends that infants should be exclusively breastfed for approximately six months, followed by introduction of complementary SF with continued breastfeeding until one year or beyond.[29] However, research shows that approximately 16% of mothers in the United States do not comply with these recommendations and introduce SF to their infants prior to 4 months, while 13% do so at ≥7 months.[30] The complexity of these factors amidst trends in infant feeding indicate the need to better understand the effects of age at SF introduction on obesity.

Thus far, studies have shown inconsistent associations between age at SF introduction and obesity. In a longitudinal survey of children born to predominantly white mothers of varying income levels in the United States, introduction of SF at ≥6 months compared to <4 months was associated with significantly lower weight-for-age Z scores at one year of age.[31] In another cohort study among predominantly high income families in Australia, introduction to SF at >3 months versus ≤2 months was associated with a lower odds of overweight/obesity at two years of age.[32] Moreover, in a longitudinal analysis of Caucasian mother-child dyads in Australia, delaying introduction of SF was associated with a lower odds of overweight/obesity at 10 years of age per week of delay.[33]

On the other hand, delaying SF introduction beyond five months (versus <5 months) was associated with higher body mass index (BMI) at one, two, three and six years of age among a cohort of mostly white infants enrolled in a prospective study in the United States within one week of birth.[34] In addition, one cross-sectional study in Australia suggested that introduction of SF at four months or at ≥7 months, compared to introduction of SF at 6 months, was associated with higher odds of having a BMI >97.7th percentile at two years of age among infants of varying socioeconomic backgrounds.[35] Based on cross-sectional data from eight European countries, introduction of SF at ≥7 months versus 4-6 months was also associated with a higher odds of overweight/obesity at 2-9 years among children of parents with medium to high educational level based on the International Standard Classification of Education.[36]

Some research in Australia and the United States demonstrated that the relationship between age at which SF is introduced and obesity differs by infant feeding status, with adverse effects mostly seen among formula-fed infants or those breastfed for a short duration (<4 months).[35,37] One study in China showed that there was no clear association between SF introduction at <3 versus 5-6 months of age and overweight/obesity in infancy, signifying that these results may not be consistent in a non-Western setting.[38] Other research revealed similar null results for the association between age at SF introduction and overweight and obesity in childhood and adolescence after adjustment for covariates.[39,40] As such, despite some evidence linking both early and late SF introduction to childhood obesity, further evidence is needed to clarify this association and to assess whether effects persist across the life course. Therefore, in chapter one, I evaluate the effects of age at SF introduction on risk of obesity in childhood, adolescence and adulthood.

TELEVISION VIEWING AND PHYSICAL ACTIVITY IN EARLY AND LATE CHILDHOOD

TVs, computers, smartphones and video games are common forms of screen media use among children globally.[41,42] Although the American Academy of Pediatrics recommends that children's screen time should be limited to <1-2 hours per day,[43,44] internationally representative statistics reveal 34-79% of children engage in >2 hours of daily screen time.[42] TV viewing remains the most popular form of screen time, although other types of screen use are steadily rising.[41]

Physical inactivity is generally thought to be interrelated with sedentary screen-based behaviors – i.e. time spent in front of a screen is likely time that is not spent being physically active.[45] Some studies support this connection by showing that children who had high TV viewing were at increased risk of not reaching the appropriate moderate-to-vigorous PA level, compared to those with less TV viewing.[46,47] By this reasoning, reducing screen time could result in increasing time spent engaging in PA. However, opposing research has demonstrated that low screen time does not necessarily translate into high PA.[48] This evidence suggests that screen time and PA may not lie on opposite ends of the same spectrum, and thus may have independent effects on health. Nonetheless, both screen time and PA are behaviors established in childhood that may track throughout adolescence and adulthood.[49,50] They may also be associated with health outcomes, such as overweight and obesity, that could persist throughout life.

Much of the literature confirming a positive association between screen time, specifically TV viewing among children, and overweight/obesity has been based on cross-sectional studies.[51,52] These associations held across ethnicities, with associations seen in studies conducted in Iran,[53] China,[54] and Colombia.[55] Other studies showed null associations between measures of screen time and obesity.[56,57]

Cross-sectional studies make it difficult to discern whether the association between screen time and obesity is temporal or driven by reverse causality – i.e. children who are obese may choose to watch more TV, rather than more TV viewing leading to obesity. As such, evidence from longitudinal studies may be more appropriate to shed light on the proposed temporal relationship between screen time and obesity. Thus far, prospective studies with only a few years of follow-up are in accord with the positive correlation seen between high screen time and obesity from cross-sectional data;[56,58] while others suggest a null association.[57]

Despite the overabundance of research on screen time and obesity, few longitudinal studies have assessed the long-term effects of TV viewing in childhood on obesity across the life course. For example, in one birth cohort study of participants of primarily European descent and representative socioeconomic status' in New Zealand, weeknight TV viewing at 5-15 years was a significant predictor of higher BMI at 26 years.[59] Similarly, in a follow-up of the 1970 British birth cohort, each additional hour of weekend TV viewing at age five was associated with a higher risk of obesity by age 30 among white participants after adjusting for socioeconomic status and other covariates.[60] Moreover, adolescents of various ethnicities and household income levels in the United States who had 40 versus 4 hours of screen time/week had a higher odds of incident obesity in young adulthood; effects were stronger when combined with low moderate-to-vigorous PA bouts.[23]

Assessing changes in anthropometric trajectories over extended periods of time may provide useful insight into how individual weight and BMI are altered by sedentary behaviors such as TV viewing at critical periods. Few studies have examined the effect of TV viewing on trajectories for indicators of obesity. In one study in the United States, TV viewing for >3 hours versus <1.75 hours/day among preschool children from predominantly white, middle class families was associated with an increase in BMI and body fat from 4 to 11 years of age. These effects were exacerbated when combined with either low PA or a high fat diet.[22] TV viewing was also positively associated with fat mass and visceral adiposity over time from ages 5-19 years in another study of mostly white individuals with high socioeconomic status in the United States.[61] In the 1958 British birth cohort, frequent TV viewing in adolescence and early adulthood was associated with greater BMI gains into mid-adulthood, with a greater waist-to-hip ratio among those who watched TV ≥5 versus <5 times/week.[62] In contrast, in a prospective study of Australian adults, increasing versus decreasing TV viewing over a 5-year period in adulthood was not associated with increases in waist circumference across a 12 year period.[63] Also, exceeding (>2 hours/day) versus meeting (≤2 hours/day) screen time recommendations for age was not associated with greater increases in BMI over 3 years among Indigenous Australian Children.[64] Thus, there is conflicting evidence for an association between TV viewing in childhood and obesity later in life, especially pertaining to anthropometric trajectories over time.

Given what we know about tracking of behaviors and biological outcomes from childhood to adulthood, it is important to assess the long-term effects of TV viewing in early life with outcomes across the life course. As such, chapter 3 focuses on the independent effects of TV viewing in childhood and the joint effects of TV viewing and PA in childhood on obesity incidence across the life course. Chapter 4 examines the effects of TV viewing in childhood on anthropometric trajectories from childhood through adolescence.

ADDRESSING GAPS IN THE LITERATURE

The rates of obesity in children, adolescents and adults are disturbingly high.[6,7] Although these numbers have plateaued in recent years, projections from 2008 anticipated that rates of obesity would double in children by 2030 and that all Americans would become overweight/obese by 2048.[65] Consequently, a life course epidemiology approach may identify risk factors for obesity across an individual's life course, thus lending support for interventions during target periods which may be more effective at reducing risk of disease than interventions later in life.

Limited inconsistent findings appear for age at SF introduction and childhood obesity; few have tracked the effects of this exposure throughout life. Moreover, although studies have established that sedentary behaviors such as TV viewing and physical inactivity are associated with obesity cross-sectionally or proximally to the exposure, there is inadequate evidence for the persistence of such behaviors in childhood on obesity later in life, on changes in weight and BMI trajectories over time or on waist circumference and waist-to-height ratio in adolescence. The following dissertation aims were developed to address these gaps in the effects of early life exposures on obesity throughout the life course.

SPECIFIC AIMS

Specific aim 1: the first aim of this dissertation utilizes linked data from the Nurses' Health Study II and the Nurses' Mothers' Cohort Study to examine the association between age at SF introduction in infancy and risk of obesity in childhood, late adolescence and adulthood in female nurses. The hypothesis states: both early (<3 months) and late (≥9 months) introduction of SF will be associated with higher risk of obesity across the life course, compared to SF introduction at 6-9 months. The findings for this Aim are presented in Chapter 2.

Specific aim 2: the second aim uses the same maternal-nurse daughter dyads from the first aim to examine the effects of TV viewing in childhood alone, and in combination with PA in childhood, on overweight and obesity across the life course. The hypothesis states: girls who watched TV for two or more hours per day at 3-5 and 5-10 years, compared to no TV, will be at increased risk of overweight and obesity throughout life. The joint effects of high TV viewing and low PA, versus low TV viewing and high PA, will result in higher risk for overweight and obesity throughout the life course.

Specific aim 3: the third aim is tested in a nested case-control study with follow-up of offspring of pre-eclamptic and normotensives within a prospective cohort of births between January 1993 and December 1995 in Stavanger, Norway. This aim examines the effect of TV viewing in childhood on change in BMI and weight Z-scores from childhood to adolescence, and on waist circumference and waist-to-height ratio Z-scores in adolescence in boys and girls. The hypothesis states: children who have two or more hours of TV viewing per day at 3-6 years, versus half an hour or less per day, are likely to have greater increases in BMI and weight Z-scores from 4 to 12.8 years and higher waist circumference and waist-to-height ratio Z-scores at 10.8/11.8 and 12.8 years.

Chapter 2: Age at Solid Food Introduction and Obesity Throughout the Life Course

ABSTRACT

Obesity has until recently been increasing alarmingly with early life diet potentially influencing its development. Limited studies have assessed the association between age at solid food (SF) introduction and childhood obesity with equivocal results; fewer have tracked the consequence of this exposure into late adolescence or adulthood. This study aims to examine the association between age at SF introduction and obesity throughout the life course. Among 31,816 mother-nurse daughter dyads in the Nurses' Mothers' Cohort Study and the Nurses' Health Study II, information was collected on age at SF introduction, body somatotype at ages 5 and 10 and body mass index (BMI) at age 18 and in adulthood. Odds ratios (ORs) and 95% confidence intervals (95% CIs) for obesity throughout life were estimated using logistic regression models with adjustment for parental and nurse daughter covariates. Nurse daughters introduced to SF at ≥9 versus 6-9 months had marginally higher age-adjusted (OR: 1.21, 95% CI: 1.01, 1.47) and covariate-adjusted (OR: 1.22, 95% CI: 1.01-1.47) odds of obesity at age 5. Age at SF introduction was not related to obesity at ages 10 and 18 or in adulthood. In conclusion, late age at SF introduction was marginally associated with obesity at age 5, but this association did not persist throughout the life course.

Keywords: solid foods, complementary foods, infant feeding, obesity, childhood

INTRODUCTION

Obesity, a global epidemic and leading public health challenge, affects 9.4% of children aged 2-5 years, 17.4% of children aged 6-11 years, 20.6% of adolescents aged 12-19 years and 37.7% of adults in the United States.[7,8] Obesity may track throughout the life course[9] and is associated with a myriad of conditions including cardiovascular disease, type 2 diabetes, metabolic syndrome, joint problems, reduced life expectancy and poorer psychological state.[11] Obesity is a multifaceted disorder with an interplay among genetic, dietary and hormonal factors contributing to its development early in life.[66] As such, exposures during infancy may program metabolic health later in life and prevention efforts could begin early.

Drawing on the hypothesis that early life exposures may determine later health and disease, age at introduction of solid food (SF) may be an early modifiable risk factor for obesity. The American Academy of Pediatrics (AAP) currently recommends exclusive breastfeeding for about 6 months, followed by complementary feeding with continued breastfeeding until 1 year and beyond as mutually desired by the mother and infant.[29] However, approximately 40% of mothers in the United States do not comply with these recommendations and introduce SF to their infants earlier than 4 months of age, while 7% introduce SF at or after 6 months of age.[30] Therefore, it is important to determine whether age at SF introduction is associated with obesity across the life course in a cohort of mother-offspring dyads.

Studies evaluating the association between age at SF introduction and obesity have inconsistent results. Research has shown higher odds of increased weight-for-age in infancy[31] and childhood overweight and obesity[32,33] with earlier SF introduction, while other studies demonstrated null associations in childhood and adolescence.[38,40] Results from one study indicated the association between early SF introduction and childhood obesity only existed among formula-fed infants.[37] Other research suggested that delayed introduction of SF beyond 6 months may in fact increase risk of childhood obesity.[35,36]

Several of these studies were limited by their relatively small sample sizes and an inability to adjust for multiple confounding variables or track results into adolescence or adulthood. Therefore, our aim was to evaluate the association between age at introduction of SF and obesity at different stages of the life course using a large ambidirectional cohort study with exposure and outcome data from two independent sources and adjustment for potential confounders.

METHODS

Study Population

The Nurses' Health Study II (NHS II) is a prospective cohort study of 116,430 female registered nurses aged 25-42 years in 1989 (baseline) and followed biennially. At baseline, nurses self-reported their medical and reproductive history and health behaviors. Updates on lifestyle, diet and clinical data were provided every 2 years with a 90% response rate for each 2-year interval. The Nurses' Mothers' Cohort Study has the mothers of the nurses in the Nurses' Health Study I and II who retrospectively reported early life exposures of their nurse daughter. In 2000, a total of 52,155 questionnaires were mailed to mothers of nurses who were willing to participate along with a prepaid return envelope. Approximately 77% of the mailed questionnaires were completed and returned (n=39,904) to the Brigham and Women's Hospital, Channing Laboratory.[67] Maternal and nurse daughter data were linked to obtain exposure and outcomes for the nurse, forming an ambidirectional cohort study design. Analyses were restricted to participants in the NHS II whose mothers completed and returned the Nurses' Mothers' Cohort Study questionnaire (n=35,830). Nurses who were: adopted or had an unknown adoption status (n=1895); twins (n=561); and missing exposure (n=562) and outcome (n=996) data were excluded from the analyses, yielding a final sample size of 31,816 mother-nurse daughter dyads. The study protocol was approved by the Institutional Review Boards of the National Cancer Institute, Bethesda, Maryland, the Brigham and Women's Hospital and Harvard School of Public Health, Boston, Massachusetts and The University of Texas at Austin, Austin, Texas.

Age at solid food introduction

The age at which SF was introduced to the nurse daughters was ascertained via the Nurses' Mothers' Cohort Study questionnaire. Mothers were asked to recall: "At what age did you start feeding this daughter SF?" Response categories were "before 3 months of age," "3-6 months of age," "6-9 months of age," or "9 months of age or older." Age at SF introduction at 6-9 months was chosen as the referent category based on current recommendations for age at SF introduction.[68,69]

Ascertainment of obesity

To assess childhood obesity, nurses were asked to recall their body somatotype at different stages of their life (ages 5 and 10) on the 1989 baseline questionnaire using a 9-

level pictogram with body somatotypes/shapes ranging from 1 being the leanest to 9 being the most overweight (Figure 2.1).[70] Given the limited number of nurses reporting somatotypes on the higher end and in accordance with prior research utilizing this scale, a somatotype of 5 or greater was defined as having “above healthy weight” or obesity.[71,72]

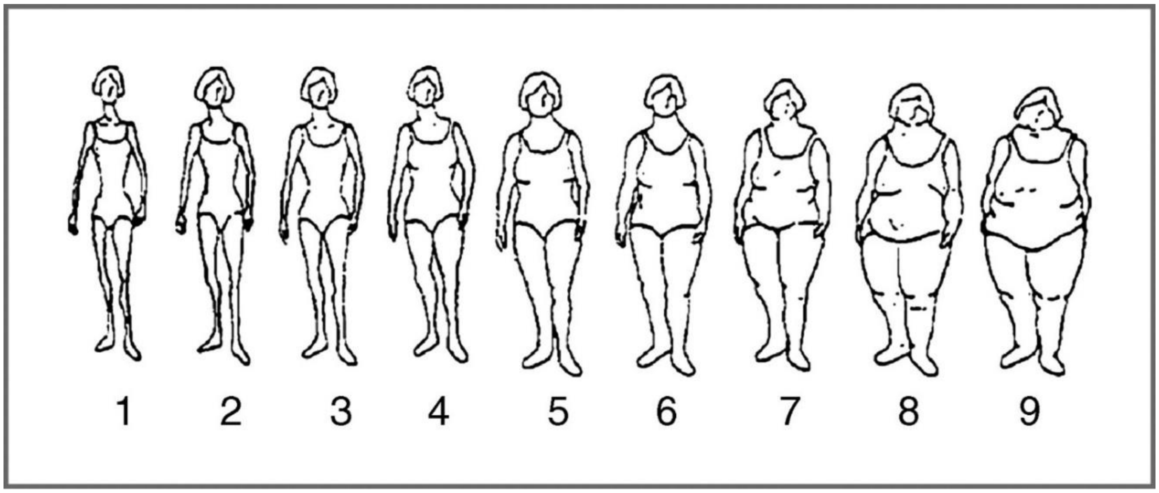


Figure 2.1. Images Used to Assess Body Somatotype at Ages 5 and 10 Years in the Nurses’ Health Study II in 1989[70]

Evidence supporting use of the same somatotypes as indicators of obesity was demonstrated in earlier research. In follow up of the longitudinal Third Harvard Growth Study, the correlation among females aged 71-76 years who recalled somatotype at age 5 and their Body Mass Index (BMI) based on weight and height directly measured at age 5 was 0.60.[73] For age 10, the correlation between the somatotypes and measured BMI was 0.65. In a study by Must et al., the Pearson correlation coefficient between BMI percentile at menarche and recalled body somatotype at menarche was 0.61.[74] Predictive validity was demonstrated by the positive association between increasing childhood somatotype and type 2 diabetes among nurses.[72]

Weight at age 18 and weight and height in 1989 (ages 25-42 years/adulthood) were self-reported on the NHS II 1989 baseline questionnaire. Weight at age 18 and height in 1989 were used to assess BMI at age 18; weight and height in 1989 were used to assess BMI in adulthood.[75] The National Heart, Lung, and Blood Institute classification of BMI was followed with underweight (<18.5 kg/m^2), normal weight (18.5 kg/m^2 – 24.9 kg/m^2), overweight (25.0 kg/m^2 – 30.0 kg/m^2) and obesity (≥30.0 kg/m^2).[76] In a study of 140 Nurses' Health Study I participants, the Pearson correlation coefficient between self-reported weight and the average weight measured by 2 trained technicians following adjustment for age and within-person variability was 0.97.[77] Moreover, records of physical examinations conducted on 118 NHS II participants upon entry to college or nursing school were compared to self-reported weight at age 18 and current height. The correlation coefficients between measured weight and height from records and recalled weight and reported current height were 0.87 and 0.94, respectively.[78] Therefore, there appears to be high validity of recalled weight and self-reported height in this cohort.

Statistical Analyses

The sample was characterized using frequencies, percentages, measures of central tendency (mean ± standard deviation) and graphical analyses, and data are presented by somatotype at age 5. $\chi 2$ tests were computed to evaluate differences in participant characteristics between somatotypes. Trends in age at SF introduction were assessed via cross-tabulations with covariates. Binomial logistic regression models were applied to estimate the odds ratios (ORs) and 95% confidence intervals (95% CIs) of obesity at ages 5 and 10 (somatotype ≥5 compared to <5) and at age 18 and in adulthood (BMI ≥30kg/m^2

compared to <30kg/m^2) by age at SF introduction adjusted for age of nurses at baseline. This was done to account for potential recall bias due to the age range of the nurses at the time of questionnaire return. Models at age 5 were then adjusted for the following parental and nurse daughter potential predictors of obesity (chosen *a priori*): maternal and paternal education (<12, 12, 13-15, ≥16 years), maternal pre-pregnancy BMI and paternal BMI at nurse's birth (12-<18.5, 18.5-<25, 25-<30, ≥30 kg/m^2) maternal gestational weight gain (<10, 10-14, 15-19, 20-29, 30-40, >40 lbs), maternal smoking during pregnancy (non-smoker, quit during pregnancy, smoked 1-14 cigarettes/day, smoked ≥15 cigarettes/day), maternal activity during pregnancy (highly active, somewhat active, mostly inactive/inactive), maternal gestational diabetes (yes, no), family history of diabetes (yes, no), maternal age at nurse's birth (<20, 20-<25, 25-<30, 30-<35, 35-<40, ≥40 years), home ownership at nurse's birth (yes, no), nurse's birthweight (<5.5, 5.5-<6.9, 6.9-<8.8, 8.8-<10, ≥10 lbs), nurse's gestational age (32-<37, 37-<40, 40-<43, ≥43 weeks), nurse's birth cohort (1946-1949, 1950-1954, 1955-1959, 1960-1964), nurse's breastfeeding duration (not breastfed or <1 week, <3 months, 3-<6 months, 6-<9 months, 9-<12 months, ≥12 months), type of SF first introduced to nurses (cereals, fruits, vegetables, and breads/crackers/cookies), nurse's PA at ages 3-5 years (highly active, active, mostly inactive/inactive) and nurse's daily screen time at ages 3-5 years (none, 0.5-1, 2, 3, ≥4 hours). At age 10, nurse's PA at ages 5-10 years (highly active, active, mostly inactive/inactive) and nurse's daily screen time at ages 5-10 years (none, 0.5-1, 2, 3, ≥4 hours) were also added as potential covariates. At age 18, age 5 and 10 covariates and nurse's age at menarche (<12, 12, 13, 14, >14 years), activity during high school (never, 1-3, 4-6, 7-9, 10-12 months/year) and cigarettes smoked at <15 and 15-19 years (never, 1-14 cigarettes/day, ≥15 cigarettes/day) were added as potential confounders. In adulthood, nurse's age at menarche, smoking status (never, past, 1-14 cigarettes/day, ≥15 cigarettes/day) and activity level during the past year in 1989 (<3, 3-<9, 9-<18, 18-<27, 27-<42 and ≥42 METS/week) were included as potential covariates in addition to age 5 and 10 covariates. Missing indicators were used for participants with missing covariate information.

Secondary analyses of obesity at age 18 and in adulthood were conducted using BMI as a continuous variable in a linear regression model adjusted for the aforementioned covariates. Interactions between age at SF introduction and birth year, breastfeeding duration, infant feeding status (breastfed to 9 months versus never breastfed), and content of the bottle (canned evaporated milk, soy-based infant formula or commercial infant formula) in relation to obesity at ages 5, 10, 18 and in adulthood were also tested by entering both variables and an interaction term between them in logistic regression models. Lastly, binomial logistic regression models were considered by infant feeding status to assess differences in the association between age at SF introduction and obesity among nurses breastfed to 9 months versus those not breastfed (i.e. formula-fed). All analyses were completed using SAS 9.4 (SAS Institute Inc, Cary, NC, USA).

RESULTS

Parental and nurse daughter characteristics (n=31,816) are presented in Table 2.1 by somatotype at age 5; 22%, 33%, 25%, 13% and 6% of nurses classified themselves into somatotypes 1 through ≥5 at age 5, respectively. The highest percentage of mothers had 12 years of education, a pre-pregnancy BMI between 18.5-<25 kg/m^2, gained 20-29 lbs of weight during pregnancy, were non-smokers and were active during pregnancy. The average maternal age at nurse's birth was 26.3 ± 4.9 years. Likewise, the highest percentage of nurses' fathers had a normal BMI and had 12 years of education at the nurse's birth. Fifty two percent of nurse's parents did not own homes at the nurse's birth. The average birthweight for nurses was 6.8 ± 1.1 lbs with a mean gestational age of 39.8 ± 2.6 weeks. Roughly 34% of nurses were born 1955-1959, 41% were breastfed, 92% had cereal as a first food, 64% were active at ages 3-5 years and 70% had 0.5-2 hours of screen time daily at ages 3-5 years. Maternal age and education at nurse's birth, pre-pregnancy BMI, gestational weight gain, activity during pregnancy; family history of diabetes; paternal education and BMI at nurse's birth; nurse's birthweight, gestational age, birth year, breastfeeding duration, type of SF first consumed and PA and screen time at ages 3-5 years differed significantly by nurse's somatotype at age 5 ($p<0.05$).

Table 2.1. Demographic and lifestyle characteristics of nurse daughters and their parents by daughter's somatotype at age 5 (n=31,816)

	Somatotype 1 (n=7061)	Somatotype 2 (n=10475)	Somatotype 3 (n=8073)	Somatotype 4 (n=4187)	Somatotype ≥5 (n=2020)
	%				
Maternal education at nurse's birth (years)					
<12	16.2	12.5	12.0	13.4	14.8
12	53.2	50.1	48.2	49.3	50.0
13-15	22.4	26.6	27.7	26.3	25.8
≥16	8.2	10.9	12.2	11.0	9.5
Maternal pre-pregnancy BMI (kg/m^2)					
12 - <18.5	13.4	11.1	8.4	6.7	6.4
18.5 - <25	81.3	83.2	84.5	84.2	82.3
25 - <30	4.6	4.9	6.3	8.0	9.7
≥30	0.8	0.7	0.8	1.1	1.6
Maternal gestational weight gain (lbs)					
<10	3.7	3.8	3.2	3.4	3.8
10-14	12.1	11.0	10.9	11.0	11.8
15-19	21.5	21.5	21.1	19.2	18.3
20-29	41.9	42.8	42.6	41.6	40.0
30-40	15.8	16.3	17.2	18.5	20.1
>40	5.1	4.6	5.1	6.3	6.2
Maternal smoking during pregnancy[1]					
Non-smoker	75.6	76.0	75.5	74.2	72.5
Quit during pregnancy	4.2	3.9	4.1	4.0	4.3
1-14 cigarettes/day	12.5	12.0	12.7	13.1	14.4
≥15 cigarettes/day	7.8	8.2	7.7	8.6	8.9
Maternal activity during pregnancy					
Highly active	27.0	27.1	27.4	25.7	23.9
Active	64.5	63.9	64.3	66.2	67.0
Mostly inactive/inactive	8.5	9.1	8.3	8.1	9.1
Maternal gestational diabetes (yes)	0.5	0.3	0.5	0.6	0.4
Family history of diabetes (yes)	25.0	22.5	23.5	25.0	26.0
Maternal age at nurse's birth (years)					
<20	5.5	5.1	4.9	4.8	4.9
20 - <25	37.5	35.5	35.3	33.8	34.0
25 - <30	34.8	36.0	35.9	36.3	35.7
30 - <35	15.5	16.4	17.2	18.2	17.8
35 - <40	5.6	6.0	5.6	5.9	6.2
≥40	1.2	1.0	1.0	1.1	1.4

Table 2.1, cont.

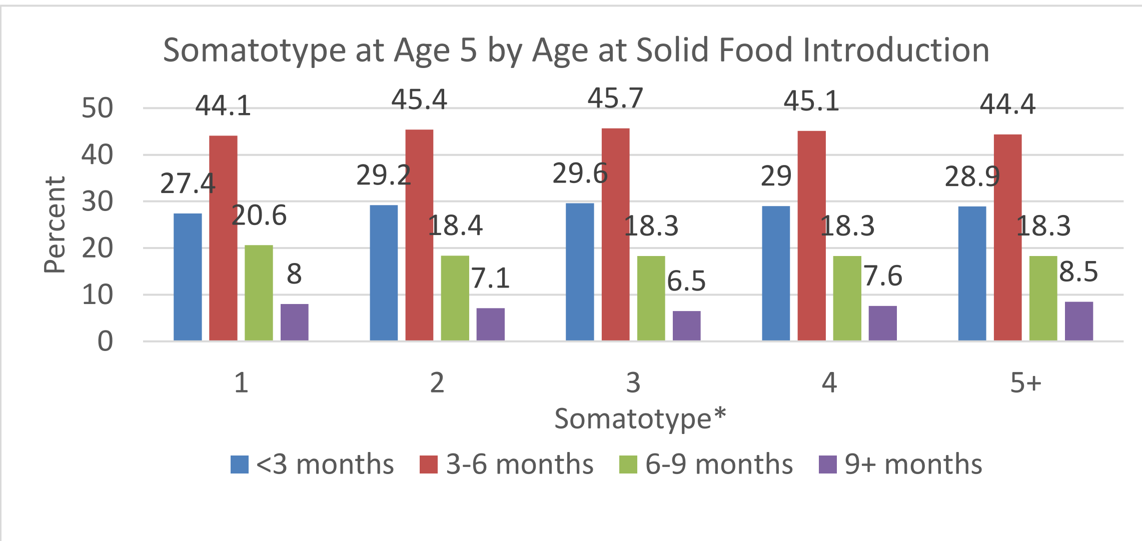
Paternal education at nurse's birth (years)					
<12	21.3	17.0	16.5	19.4	22.4
12	40.2	38.3	38.1	36.7	40.6
13-15	19.9	20.3	20.3	20.6	17.7
≥16	18.7	24.4	25.1	23.3	19.4
Paternal BMI at nurse's birth (kg/m^2)					
12 - <18.5	2.3	1.6	1.3	1.3	1.3
18.5 - <25	76.9	75.6	72.1	70.4	66.8
25 - <30	19.3	21.0	24.4	26.1	29.1
≥30	1.6	1.8	2.2	2.3	2.8
Home ownership at nurse's birth (yes)	46.2	48.5	47.8	47.8	48.0
Birthweight (lbs)					
<5.5	6.8	5.7	5.4	5.5	5.6
5.5 - <6.9	37.6	34.2	29.5	26.6	26.8
6.9 - <8.8	51.8	55.6	59.1	59.6	58.6
8.8 - <10	3.2	3.8	5.2	7.0	7.2
≥10	0.6	0.7	0.8	1.4	1.8
Gestational age (weeks)[2]					
32 - <37	5.5	4.0	3.5	4.2	3.8
37 - <40	47.7	48.3	46.3	43.8	45.4
40 - <43	36.7	36.7	39.0	39.9	38.5
≥43	10.2	11.0	11.3	12.1	12.4
Birth year					
1946-1949	16.1	12.8	13.6	13.2	15.5
1950-1954	30.5	29.4	32.1	33.9	32.8
1955-1959	33.0	35.1	34.3	34.5	33.9
1960-1964	20.4	22.8	19.9	18.3	17.8
Breastfeeding duration (months)					
Not breastfed or <1 week	60.9	58.9	56.5	57.8	61.0
<3	18.7	19.4	19.9	20.1	19.0
3 - <6	9.7	10.5	11.4	9.8	10.0
6 - <9	5.9	6.4	7.2	7.2	5.4
9 - <12	3.4	3.4	3.9	3.8	3.6
≥12	1.5	1.4	1.3	1.3	1.0
Type of solid food first introduced to nurse					
Cereal	90.2	92.2	92.2	91.9	91.6
Vegetables	3.6	2.6	2.5	2.2	2.8
Fruits	4.1	3.5	3.5	3.9	3.6
Breads, crackers or cookies	2.1	1.7	1.8	1.9	2.0
Nurse's physical activity at ages 3-5 years					
Highly active	37.1	34.1	31.6	29.1	26.8
Active	59.8	63.1	65.1	66.1	66.1
Mostly inactive + inactive	3.1	2.7	3.3	4.9	7.2

Table 2.1, cont.

Nurse's screen time at ages 3-5 years (hours)					
None	22.7	19.8	21.6	21.5	21.1
0.5-1	42.4	45.8	44.8	44.4	41.0
2	25.0	25.2	24.4	24.2	25.4
3	7.8	7.0	6.9	7.2	9.6
≥4	2.1	2.1	1.7	2.0	3.0

[1]2% missing
[2]42% missing or do not recall

The distribution of age at SF introduction was similar across somatotypes and BMI categories. Approximately 29% of mothers reported introducing SF at <3 months of age, 45% at 3-6 months, 19% at 6-9 months and 7% at ≥9 months across somatotypes 1 to ≥5 at age 5 (Figure 2.2). A decreasing trend in late age at SF introduction (≥9 months) was seen across increasing categories of gestational age, birth year and maternal education at nurse's birth, where a higher percentage of nurses born prematurely (32-<37 weeks), between 1946-1949 and with mothers who had <12 years education were introduced to SF later. These trends did not appear for other covariates (data not shown).



*Somatotypes denote "body shapes" on the 9-level Stunkard somatotype pictogram with somatotype 1 defined as being lean and somatotype 5+ defined as having obesity

Figure 2.2. Somatotype at Age 5 by Age at Solid Food Introduction

In the age-adjusted binomial logistic regression analysis, nurse daughters who were fed SF at ≥9 months had higher odds of somatotype ≥5 at age 5 (OR: 1.21, 95% CI: 1.01-1.47), compared to those introduced to SF at 6-9 months (Table 2.2). This association remained significant after adjustment for parental and nurse daughter characteristics (OR: 1.22, 95% CI: 1.01, 1.47). In the covariate-adjusted model, higher maternal pre-pregnancy BMI and paternal BMI at nurse's birth (≥25 kg/m^2), maternal gestational weight gain of 10-14 lbs and 30-40 lbs, maternal smoking during pregnancy (1-15+ cigarettes/day); nurse's birthweight (>8.4 lbs), shorter breastfeeding duration (never breastfed or <1 week), inactivity between ages 3-5 years and daily screen time between ages 3-5 years (>3 hours/day) were all independently associated with a higher odds of obesity at age 5 (Table 2.3).

At ages 10, 18 and in adulthood, no significant associations between age at SF introduction and the odds of obesity were seen in age-adjusted and covariate-adjusted models (Table 2.2). Similar null results were demonstrated in the covariate-adjusted model when BMI was considered as a continuous variable at age 18. SF introduction at ≥9 months versus 6-9 months was associated with a higher BMI in adulthood (β=0.23, 95% CI: 0.02, 0.45, P-for-trend=0.17) (data not shown).

There was no effect of an interaction between age at SF introduction and either birth year, breastfeeding duration, infant feeding status or content of the bottle on the odds of obesity across all age groups. Further, when the associations between age at SF introduction and obesity were analyzed in separate models for nurses breastfed up to 9 months and then for nurses who were never breastfed, associations were null except for a higher odds of obesity at age 5 (OR: 1.44, 95% CI: 1.04, 1.99) and in adulthood (OR: 1.40, 95% CI: 1.06, 1.83) with introduction of SF at ≥9 months versus 6-9 months among breastfed nurses after adjustment for parental and nurse covariates (data not shown).

Table 2.2. Odds ratios (ORs) and 95% confidence intervals (95% CIs) for obesity at ages 5, 10, 18 and in adulthood by age at solid food introduction

Age at solid food introduction (months)	Obese (n)	Age-adjusted OR	Covariate-adjusted OR[1]
Somatotype ≥5 at age 5			
<3	583	1.06 (0.93, 1.22)	1.08 (0.94, 1.24)
3-6	896	1.02 (0.90, 1.16)	1.04 (0.92, 1.19)
6-9	370	Reference	Reference
≥9	171	1.21 (1.01, 1.47)	1.22 (1.01, 1.47)
P-for-trend		0.19	0.21
Somatotype ≥5 at age 10			
<3	1013	0.94 (0.85, 1.05)	0.97 (0.87, 1.08)
3-6	1585	0.92 (0.84, 1.02)	0.95 (0.86, 1.05)
6-9	717	Reference	Reference
≥9	279	1.01 (0.87, 1.17)	1.01 (0.87, 1.18)
P-for-trend		0.30	0.68
BMI ≥30kg/m² at age 18			
<3	183	0.80 (0.64, 1.01)	0.85 (0.67, 1.07)
3-6	320	0.93 (0.76, 1.14)	1.02 (0.83, 1.26)
6-9	141	Reference	Reference
≥9	57	1.05 (0.77, 1.43)	0.99 (0.72, 1.37)
P-for-trend		0.17	0.28
BMI ≥30kg/m² in adulthood			
<3	859	1.01 (0.91, 1.13)	0.99 (0.88, 1.11)
3-6	1334	0.95 (0.85, 1.05)	0.98 (0.88, 1.09)
6-9	602	Reference	Reference
≥9	254	1.11 (0.95, 1.29)	1.09 (0.92, 1.28)
P-for-trend		0.13	0.62

[1]Adjusted for:

Age 5: maternal education, pre-pregnancy Body Mass Index (BMI), gestational weight gain during pregnancy, smoking during pregnancy, activity during pregnancy, gestational diabetes, age at nurse's birth; family history of diabetes; paternal education and BMI at nurse's birth; home ownership at nurse's birth; nurse's birthweight, gestational age, birth year, breastfeeding duration, type of solid food first introduced, physical activity and screen time at ages 3-5 years and age at questionnaire return (1989)

Age 10: age 5 covariates and nurse's physical activity and screen time at ages 5-10 years

Age 18: age 10 covariates and age at menarche, activity during high school and cigarettes smoked at <15 years and 15-19 years of age

Adulthood: age 10 covariates and age at menarche, activity level in 1989 and smoking status in 1989

Table 2.3. Odds ratios (ORs) and 95% confidence intervals (95% CIs) for obesity at age 5 (somatotype ≥5) by age at solid food introduction and other covariates

Variable	ORs (95% CIs)
Age at solid food introduction (months)	
<3	1.08 (0.94, 1.24)
3-6	1.04 (0.92, 1.19)
6-9	Reference
≥9	1.22 (1.01, 1.47)
Maternal education (years)	
<12	0.99 (0.86, 1.15)
12	Reference
13-15	1.11 (0.99, 1.25)
≥16	1.08 (0.90, 1.29)
Maternal pre-pregnancy Body Mass Index (BMI) (kg/m^2)	
12 - <18.5	0.66 (0.55, 0.79)
18.5 - <25	Reference
25 - <30	1.54 (1.31, 1.81)
≥30	1.62 (1.11, 2.38)
Maternal gestational weight gain (lbs)	
<10	1.09 (0.84, 1.41)
10-14	1.17 (1.00, 1.38)
15-19	0.96 (0.84, 1.10)
20-29	Reference
30-40	1.20 (1.06, 1.37)
>40	1.21 (0.98, 1.50)
Maternal smoking during pregnancy	
Non-smoker	Reference
Quit during pregnancy	1.16 (0.92, 1.46)
Smoked 1-14 cigarettes/day	1.31 (1.14, 1.50)
Smoked ≥15 cigarettes/day	1.25 (1.06, 1.47)
Maternal activity during pregnancy	
Highly active	0.90 (0.81, 1.01)
Active	Reference
Mostly inactive + inactive	0.97 (0.82, 1.14)
Maternal gestational diabetes (yes)	0.78 (0.38, 1.60)
Family history of diabetes (yes)	1.02 (0.92, 1.13)
Maternal age at nurse's birth (years)	
<20	0.98 (0.78, 1.24)
20 - <25	0.96 (0.86, 1.08)
25 - <30	Reference
30 - <35	1.07 (0.94, 1.23)
35 - <40	1.08 (0.89, 1.33)
≥40	1.34 (0.90, 1.98)
Paternal education at nurse's birth (years)	
<12	1.11 (0.98, 1.26)
12	Reference
13-15	0.84 (0.73, 0.96)
≥16	0.82 (0.71, 0.94)

Table 2.3, cont.

Paternal BMI at nurse's birth (kg/m^2)	
12 - <18.5	0.91 (0.61, 1.36)
18.5 - <25	Reference
25 - <30	1.42 (1.28, 1.58)
≥30	1.48 (1.11, 1.96)
Home ownership at nurse's birth (yes)	0.99 (0.90, 1.10)
Birthweight (lbs)	
<5.5	1.09 (0.92, 1.29)
5.5 - <6.9	Reference
6.9 - <8.8	1.27 (1.12, 1.42)
8.8 - <10	1.86 (1.51, 2.29)
≥10	2.42 (1.67, 3.50)
Gestational age (weeks)	
32 - <37	1.04 (0.75, 1.45)
37 - <40	Reference
40 - <43	0.93 (0.64, 1.36)
≥43	0.90 (0.44, 1.84)
Birth year	
1946-1949	Reference
1950-1954	1.00 (0.82, 1.22)
1955-1959	1.01 (0.73, 1.40)
1960-1964	0.94 (0.59, 1.51)
Breastfeeding duration (months)	
Not breastfed or <1 week	1.53 (0.97, 2.42)
<3	1.44 (0.90, 2.29)
3 - <6	1.47 (0.91, 2.36)
6 - <9	1.23 (0.75, 2.01)
9 - <12	1.39 (0.83, 2.32)
≥12	Reference
Type of solid food first introduced to nurse	
Cereal	1.02 (0.77, 1.35)
Vegetables	Reference
Fruits	0.98 (0.68, 1.41)
Breads, crackers or cookies	1.05 (0.69, 1.61)
Nurse's physical activity at ages 3-5 years	
Highly active	0.78 (0.71, 0.87)
Active	Reference
Mostly inactive + inactive	1.92 (1.59, 2.32)
Nurse's screen time at ages 3-5 years (hours)	
None	0.90 (0.77, 1.04)
0.5-1	0.91 (0.81, 1.02)
2	Reference
3	1.23 (1.03, 1.47)
≥4	1.33 (1.00, 1.77)

DISCUSSION

In this large cohort of mother-nurse daughter dyads from the Nurse's Mothers Cohort study linked to the Nurses' Health Study II, we report that late age at SF introduction was marginally associated with obesity at age 5, but this effect did not persist throughout the life course. These results, taken together with our previous work demonstrating a borderline association between exclusive breastfeeding for >6 months and reduced risk of somatotype ≥5 at age 5 but no association later in life,[67] suggest that infant feeding practices were not strongly associated with obesity risk during the nurses' birth cohorts and their life course.

Although several studies between 1990-2010 have reported an effect of early age at SF introduction on higher odds of obesity at 10 years,[33] BMI at 2 years,[32] BMI z-scores at 3 years,[37] weight-for-age at 1 year[31] and infant weight gain from birth to 1 year,[79] two recent systematic reviews indicated no clear association between age at SF introduction and obesity, suggesting that further research is needed to inform guidelines on age at SF introduction.[20,80] Of note, several studies in the reviews compared early introduction (<3 months) to introduction at >3-5 months, excluding children who were introduced to SF even later and who may be experiencing different outcomes accordingly. Only one study utilizing the Copenhagen Perinatal Cohort assessed the long-term effect of age at SF introduction on overweight at age 42, indicating lower odds of overweight in adulthood with increasing age (in months) at introduction of meats, firm food and vegetables.[81]

Our marginal association between late age at SF introduction and obesity at age 5 is in accord with other studies.[34-37] Specifically, in a small sample (n=54) of children enrolled in a prospective cohort study within one week of birth, delaying SF introduction to later than 5 months was related to higher BMI at 3 and 6 years of age.[34] In a cross-sectional, population-based study (2007-2011), both early (4 months) and late (≥ 7 months) introduction of SF increased the odds of BMI >97.7th percentile at ages 9-15 months with odds ratios of 1.75 and of 2.64, respectively.[35] Papoutsou et al. also demonstrated a 38% higher odds of childhood overweight/obesity (ages 2-9 years) among exclusively breastfed infants with introduction of SF at ≥ 7 months of age using cross-sectional data from 8 European countries (2007-2008).[36]

The null associations between age at SF introduction and obesity at ages 10, 18 and in adulthood have been demonstrated at different ages in previous studies.[38-40,81] It is possible that 10 and 18 years of age are proximal to puberty and that the complexity of factors influencing obesity in puberty and then later in life may mask the effect of a single early indicator such as age at SF introduction.

Some studies showed that the association between age at SF introduction and obesity may be influenced by infant feeding status, with adverse effects mostly seen among formula-fed infants or those breastfed for short durations (<4 months).[35,37] In a trial of exclusively formula-fed infants introduced to SF at different ages (i.e. starting from 3 versus 6 months) differences in energy intake between early (3 months) and late (6 months) introduction did not appear, as energy from formula feeds was displaced by SF.[82] This may explain why age at SF introduction did not influence obesity risk among nurses who were formula-fed in our study.

Inconsistency and difficulty in interpreting results across studies may stem from discrepancies in study design, sample sizes, confounders, age at which outcomes were assessed, tools to report or measure data, and the definition of and cut-offs for exposures and outcomes. The definition of and cut-offs for exposures are important within this study context, as the response category ranges for our exposure variable are not concordant with current recommendations for SF introduction at around 6 months of age. Introduction of SF at 6-9 months may mean introduction anywhere between 24 and 36 weeks of age. The biological implications could be different over these 3 months and grouping them together may alter our findings. Further, although mothers were asked to report when they first introduced SF to their nurse daughter, the questionnaire did not define "age at SF introduction." This could have been perceived as the age at "first taste" of any food other than breastmilk or formula, or the age at which any food or liquid other than breastmilk or formula was introduced and was consistently given to infants. These definitions are vague in the literature with discrepancies across major health organizations.[83] Such ambiguity in definitions may lead to under or overestimation of the magnitude of the exposure depending on maternal perception and ultimately sends mixed messages to mothers regarding the optimal age for SF introduction.

Nurses in our study were born from 1946 through 1964, therefore our results have a historical context. Knowledge about recommendations by physicians at the time are more vague than the messages delivered to mothers today, although limited evidence indicates that mothers tended to introduce SF as early as 2-4 months of age during the birth years of the nurses.[27] Also, 92% of mothers reported introducing cereal as a first food, which limits our ability to directly assess the association between age of introduction of SF and obesity by types of SF. It is therefore difficult to disentangle the effect of age at SF introduction from the effect of the content of the diet consumed early in life.

The mechanism behind the observed borderline higher odds of obesity at age 5 with delayed introduction of SF at or beyond 9 months is uncertain. There appears to be a vulnerable window when delayed SF introduction, particularly at later months (e.g. ≥9 months), is associated with conditions other than childhood obesity, including pediatric acute lymphoblastic leukemia,[84] feeding problems, and reduced consumption of food groups such as fruit and vegetables.[85] Given that introduction of SF, particularly protein and fiber, enhances microbial diversity, later introduction of solids may delay development of normal and healthy gut microbiota and have a negative impact on risk of disease later in life.[86] It is unclear why mothers waited until 9 months of age to introduce SF to their infants. Our cross tabulations between age at SF introduction and gestational age, birth year and maternal education indicated a decreasing trend in the proportion of nurses fed SF at or after 9 months with increasing categories of these variables.

Strengths of our study include the use of two well-characterized cohorts with large sample sizes. Our exposure and outcome data were obtained from two independent sources (mother and nurse daughters, respectively) and although the exposure data was retrospectively collected, the overall prospective nature of the study allows for a temporal relation between age at SF introduction and childhood obesity.

Despite the plethora of confounders that were adjusted in our models of obesity, there is still the possibility that residual confounding may occur. We recognize that energy intake is an important contributor to obesity. Although we do not have information on energy intake at ages 5 and 10, we adjusted for type of SF first introduced to infants – predominantly cereal, an energy-dense food. No information on energy intake at age 18 was collected and adulthood dietary intake was not collected until the 1991 follow-up questionnaire and thus was also not included as a covariate in our sample. Generalizability of the results to other races/ethnicities and men is not permitted given 97% of the nurses are Caucasian white women. While maternal and nurse's reporting of the exposure and outcomes respectively may be subject to recall bias, research in numerous countries has indicated that mothers are able to reliably recall infant feeding data in the short[87] and long-term,[88,89] and recall of body somatotype has been previously validated as aforementioned above.[73,74,90] Aside from the potential recall bias associated with the outcome, there is also a possibility of misclassification of nurses into body somatotypes that may not look drastically different.

Obesity involves an interaction of factors in prenatal and early postnatal life, with potential tracking in adulthood. Results from our study may add insight to the role of age at SF introduction on early life and later adiposity, but also confirm well-known and emerging prenatal and early postnatal risk factors for the condition (Table 2.3), which is consistent with other research.[32,91,92] The magnitude of the effect of late age at SF introduction on childhood obesity is relatively small, compared to the effect of high maternal pre-pregnancy BMI and paternal BMI at birth, maternal smoking during pregnancy, high birthweight and physical inactivity in childhood. This suggests that infant feeding practices may be important for healthy growth and development, but prime modifiable factors appear earlier with maternal and paternal BMI and maternal smoking during pregnancy to reduce population obesity rates. Interventions might consider incorporating a holistic host of modifiable risk factors, with a focus on exposures that are likely to have the largest effects on curbing obesity rates across the life course. Further research is needed to replicate our results in a cohort born more recently in time than the nurses, with more clear definitions of and discrete cut-offs for age at SF introduction.

CONCLUSIONS

In conclusion, our data suggest that late age at SF introduction only slightly influenced women's odds of having obesity in childhood, with no effects extending throughout life. Additional research is needed to replicate these results in more recent birth cohorts and to assess the dynamic influence of age at solid food introduction and early life diet on the obesity epidemic.

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Chapter 3: Television Viewing in Childhood and Overweight and Obesity Throughout the Life Course

ABSTRACT

Few studies address the association between television (TV) viewing in childhood and overweight/obesity throughout the life course. Among 30,921 mother-daughter dyads from the Nurses' Mothers' Cohort and the Nurses' Health Study II, the following information was collected: daughter's TV viewing and physical activity (PA) at ages 3-5 and 5-10, somatotype at ages 5 and 10, and body mass index at age 18 and in adulthood (ages 26-45). Using multivariable-adjusted logistic regression models, TV viewing for ≥4 hours/day versus no TV at ages 3-5 was associated with odds ratios of overweight/obesity of 1.61 (95% confidence interval (CI): 1.20, 2.17) at age 5, 1.46 (95% CI: 1.14, 1.86) at age 10, 1.31 (95% CI: 1.00, 1.70) at age 18 and 1.32 (95% CI: 1.10, 1.59) in adulthood. A composite variable of high TV/low PA versus low TV/high PA at ages 3-5 was associated with odds ratios of overweight/obesity ranging from 3.22 (95% CI: 2.23, 4.65) at age 5 to 1.82 (95% CI: 1.36, 2.45) in adulthood. Similar findings appeared for associations at ages 5-10. Long hours of TV viewing in childhood alone and in combination with low PA were consistently associated with higher odds of overweight/obesity across the life course.

Keywords: television viewing, screen time, overweight, obesity, life course

INTRODUCTION

Sedentary screen-based behaviors are popular among children[42,93] and may track through adolescence[49,94] and adulthood.[95] High youth screen time has been associated with adverse health outcomes,[96-99] including overweight/obesity.[100,101] Although several studies indicated a positive association between screen time, primarily television (TV) viewing, and higher body mass index (BMI), body fat and obesity in children,[47] adolescents[102] and adults,[103] others revealed no association.[57,104] Further, in two recent reviews of predominantly cross-sectional studies, the association between screen time and adiposity was weak,[105,106] suggesting that prospective cohort studies may clarify this link and the magnitude of the association. While some longitudinal evidence reported that TV viewing at ages 4-5 was associated with change in BMI from ages 4 to 11 and with incident obesity at age 30,[22,60] further studies with long follow-up periods can assess lifelong consequences of this exposure on overweight/obesity.

TV viewing has been the predominant source of screen time among children from the 1950's to the present in the United States[107]. This study therefore aims to examine the relation between hours watching TV daily during childhood and risk of overweight/obesity throughout the life course. An ambidirectional cohort design with independent sources reporting the exposure and outcome framed this research, which also assesses the joint effects of childhood TV viewing and physical activity (PA) on overweight/obesity.

METHODS

Study population

The study includes data from two cohort studies: The Nurses' Health Study (NHS) II and the Nurses' Mothers' Cohort. The NHS II, a prospective cohort of 116,430 female nurses across the US established in 1989, aims to examine the relation between dietary and lifestyle habits and risk of disease with health-related updates every 2 years. The nurses are predominantly non-Hispanic white aged 25-42 years at baseline.

The Nurses' Mothers Cohort, a retrospective cohort study, is comprised of the mothers of the nurses in the NHS I and II who reported data on themselves, the biological father and the early life exposures of their daughters (born 1946-64). A total of 52,155 questionnaires were sent to mothers who were alive, healthy and willing to participate in 2000. Of the 39,904 questionnaires returned in 2001 (76.5%), the majority (n=35,349) were mothers of nurses in the NHS II (average age at maternal questionnaire return = 72 years); analyses were restricted to these participants.[67] Mother-daughter dyads were formed by linking retrospectively recalled exposure data from the mothers in the Nurses' Mothers' Cohort and prospective outcome data reported by the daughters in the NHS II to form an ambidirectional cohort design. Daughters who were adopted or whose adoption status was unknown (n=1778), and who were missing exposure (n=569) or outcome data (n=2081) were excluded from analyses. The final sample size had 30,921 mother-daughter dyads. The study protocol was approved by the Institutional Review Boards of the Brigham and Women's Hospital and Harvard School of Public Health, Boston, Massachusetts, the National Cancer Institute, Bethesda, Maryland and The University of Texas at Austin, Austin, Texas.

Television viewing and physical activity during childhood

Daughter's childhood TV viewing was recalled by their mothers who were asked: "Between the ages of 3 and 5 years, how many hours per day during the week did your nurse daughter watch TV?" Response categories were "No TV," "up to 0.5 hours/day," "1 hour/day," "2 hours/day," "3 hours/day," "4 hours/day," and "5 or more hours/day." To account for limited responses in the upper category (5+ hours/day), this response was combined with responses for "4 hours/day." The question is based on a similar self-report question in the Youth Risk Behavior Survey which was moderately correlated with self-reported weekly viewing diaries (r=0.5) and had fair test-retest reliability (r=0.3) when the same question was completed one week apart.[108,109] Daughters were aged 3-5 years during the years 1949-1969. The same question was repeated to assess the daughter's TV viewing at ages 5-10; upper categories were combined in a similar manner. These exposures were analyzed separately to assess potential windows of vulnerability.

Mothers reported PA levels of their daughters between the ages of 3-5 and 5-10 years by answering the following question at both ages: "How would you best describe your nurse daughter's activity level compared to other girls of similar age?" Response categories were: "highly physically active," "active," "mostly inactive," and "inactive." The question was extracted from the "Stanford Brief Activity Survey" which was validated for older adults.[110] In a population-based cohort, low PA ("mostly inactive/inactive") was associated with atopic sensitization, atopic dermatitis and asthma in late childhood, demonstrating predictive validity of the question.[111]

Assessment of overweight and obesity

Childhood overweight/obesity (ages 5 and 10) was recalled by the daughters on the baseline NHS II questionnaire. A 9-level Stunkard pictogram with body shapes ranging from lean (somatotype 1) to obese (somatotype 9) was used.[70] Somatotypes ≥5 were categorized as "overweight/obese" in accord with previous research due to limited responses on the upper end of the pictogram.[72,112] This pictogram has been validated in follow up of the Third Harvard Growth Study whereby body sizes at ages 5 and 10 recalled by females aged 71-76 were correlated with BMI calculated from measured weight and height at the same ages (r=0.60-0.65).[73] Similar correlations appeared between recalled body size and BMI percentile at menarche.[74] Greater childhood somatotype was also positively associated with Type 2 Diabetes, suggesting predictive validity of the pictogram.[72]

Weight at age 18 and current height in adulthood (ages 26-45) were used to assess overweight/obesity at age 18; current weight and height in adulthood were used to assess overweight/obesity in adulthood. BMI was calculated with weight(kg)/height(m)^2 and the cut-off for overweight/obesity was ≥25kg/m^2. The correlation coefficient between self-reported weight by NHS I participants and average weight measured by technicians was r=0.97.[77] Also, records of measured weight and height for NHS II participants upon entry to college or nursing school were correlated with self-reported measurements. The correlation coefficients were r=0.87 between recalled weight at age 18 and measured weight from records; and r=0.94 between reported current height in adulthood and measured height from records.[78]

Statistical analyses

Characteristics of daughters and their parents were described using frequencies, percentages, means and standard deviations. Chi-square was calculated to test for differences in proportions by hours of TV viewing at ages 3-5. Spearman correlations were calculated between TV viewing and PA at ages 3-5 and adult TV viewing and PA.

Logistic regression models were used to estimate the association between hours watching TV daily at ages 3-5 and the odds ratios (ORs) and 95% confidence intervals (95% CIs) for overweight/obesity at ages 5, 10, 18 and in adulthood adjusted for age at daughter's return questionnaire. These models were then adjusted for childhood PA during the same period as TV viewing. The final models for overweight/obesity at ages 5 and 10 were adjusted for the above-mentioned covariates and parental and daughter covariates associated with overweight/obesity chosen *a priori* including: maternal education; maternal pre-pregnancy BMI and paternal BMI at daughter's birth; maternal gestational weight gain, smoking and activity during pregnancy; home ownership; and daughter's birthweight, gestational age, birth year and breastfeeding duration. In addition to these covariates, the following confounders were adjusted in the model for the odds of overweight/obesity at age 18: daughter's age at menarche; and in adulthood: daughter's age at menarche and adult smoking status, PA level, hours watching TV daily, caloric intake and Alterative Healthy Eating Index score. Two sensitivity analyses were conducted using logistic regression models. One analysis assessed the extent of the association between TV viewing at ages 3-5 and adult overweight/obesity accounted for by adult TV viewing and PA. The second analysis examined the association between TV viewing at ages 3-5 and adult obesity with adjustment for overweight/obesity at age 5 and the aforementioned age 5, 10 and adult covariates. The same analyses and covariates were utilized to assess the association between hours watching TV daily at ages 5-10 and overweight/obesity at ages 10, 18 and in adulthood. Missing indicators were used when participants had missing information on covariates.

In the next set of analyses, a variable that combined TV viewing and PA at ages 3-5 was classified according to screen time and PA guidelines as follows: 1) ≤2 hours TV/day + highly active/active (referent group) – i.e. low TV/high PA; 2) ≤2 hours TV/day + mostly inactive/inactive – i.e. low TV/low PA; 3) ≥3 hours TV/day + highly active/active – i.e. high TV/high PA; and 4) ≥3 hours TV/day + mostly inactive/inactive – i.e. high TV/low PA. The association between this composite measure and overweight/obesity at ages 5, 10, 18 and in adulthood was computed using logistic regression models with adjustment for parental and daughter covariates. A variable that combined TV viewing and PA at ages 5-10 was classified and analyzed similarly. All analyses were completed using SAS 9.4 (SAS Institute Inc, Cary, NC). All *P*-values were two-sided.

RESULTS

Descriptive characteristics of the daughter and her parents by hours watching TV daily at ages 3-5 are presented in Table 3.1. Approximately 9% and 15% of daughters watched >2 hours of TV/day at ages 3-5 and 5-10, respectively. At ages 3-5, 63% of daughters were active and at ages 5-10, 66% were active. The prevalence of overweight/obesity was 6% at age 5, 11% at age 10, 9% at age 18, and 31% in adulthood (ages 26-45). The average maternal pre-pregnancy BMI was 21.3 kg/m^2 and the average paternal BMI at daughter's birth was 23.6 kg/m^2. Eighty six percent of mothers had ≥12 years of education, 42% gained 20-29 lbs, 74% were non-smokers and 64% were active during pregnancy.

The mean birthweight of daughters was 6.8 lbs and the mean gestational age was 39.7 weeks. Sixty five percent of daughters were born between 1950-1959. Most daughters were not breastfed (59%). The average age at menarche was 12.4 years. The average age of daughters at questionnaire return was 35.5 years. Sixty eight percent of daughters never smoked; 75% reported <3 to 26 Metabolic Equivalents/week of PA; and 93% watched <3 hours of TV daily in adulthood. The average caloric intake in adulthood was 1800 kilocalories and the mean Alterative Healthy Eating Index score was 43.8. TV viewing and PA at ages 3-5 were minimally correlated (r=0.07) with adult TV viewing and PA.

Table 3.1. Parental and daughter characteristics by daughter's hours watching television daily at ages 3-5 (n=30,921)

Daughter's hours watching television daily at ages 3-5						
	No TV (n=6588)	**0.5 hours (n=3468)**	**1 hour (n=10394)**	**2 hours (n=7588)**	**3 hours (n=2265)**	**≥4 hours (n=618)**
			%			
Hours watching television daily at ages 5-10 (hours)*						
No TV	29.6	0.8	0.3	0.3	0.1	0.0
0.5	17.9	28.0	2.1	0.3	0.1	0.2
1	34.7	61.5	52.1	11.4	3.6	1.3
2	14.7	8.9	42.4	62.8	28.0	13.3
3	2.7	0.7	3.0	23.2	50.9	30.3
≥4	0.5	0.2	0.2	2.1	17.3	55.0
Physical activity at ages 3-5*						
Highly active	34.4	36.0	33.9	31.0	28.8	25.6
Active	62.1	60.9	63.4	65.1	64.7	64.4
Mostly inactive	2.5	2.5	2.0	2.9	4.9	6.3
Inactive	0.8	0.5	0.6	0.8	1.4	3.4
Physical activity at at ages 5-10*						
Highly active	30.0	32.2	30.3	27.8	25.8	25.6
Active	65.9	64.3	66.3	67.8	67.9	63.8
Mostly inactive	3.2	2.8	2.6	3.6	4.6	7.3
Inactive	0.7	0.8	0.8	0.8	1.6	3.4
Overweight/obesity at age 5*						
Somatotype ≥5	6.2	5.4	6.0	6.7	8.1	9.7
Overweight/obesity at age 10*						
Somatotype ≥5	11.2	9.4	10.5	11.8	13.8	15.2
Overweight/obesity at age 18*						
BMI 25-30 kg/m^2	7.1	6.3	6.6	7.4	8.3	10.4
BMI ≥30kg/m^2	1.9	1.5	2.1	2.5	2.9	3.2
Overweight/obesity in adulthood*						
BMI 25-30 kg/m^2	19.9	18.0	18.8	19.0	20.4	23.6
BMI ≥30kg/m^2	14.0	9.8	10.3	12.2	13.5	17.6

Table 3.1, cont.

Maternal education (years)*						
<12	18.9	11.0	10.7	11.7	16.5	23.5
12	43.2	43.7	49.1	56.3	58.9	57.1
13-15	26.4	28.9	28.1	23.3	19.0	16.7
16+	11.2	16.2	11.7	8.3	5.2	2.1
Maternal gestational weight gain (lbs)* [1]						
<10	3.9	4.0	3.5	3.1	3.2	4.7
10-14	13.3	11.8	11.4	10.0	9.3	9.1
15-19	20.9	22.2	21.0	20.4	16.9	19.0
20-29	40.4	40.5	42.9	43.0	43.9	36.1
30-40	16.4	16.4	16.3	17.9	20.3	22.5
>40	5.2	5.1	5.0	5.5	6.5	8.7
Maternal smoking during pregnancy* [2]						
Non-smoker	81.3	75.4	72.4	71.0	66.9	70.2
Quit during pregnancy	2.7	3.9	4.1	4.5	4.6	3.9
Smoked 1-15+ cigarettes/day	14.4	18.8	21.5	22.1	26.0	24.1
Maternal activity during pregnancy*						
Highly active	29.2	27.9	27.3	24.5	22.5	18.3
Active	62.8	63.5	63.6	66.3	64.6	65.5
Mostly inactive + inactive	7.4	8.1	8.5	8.7	12.1	15.2
Birth year*						
1946-1949	38.2	10.1	8.2	6.1	5.3	5.0
1950-1954	38.0	31.9	30.6	27.6	25.3	25.1
1955-1959	17.7	38.1	38.1	40.0	39.0	40.1
1960-1964	6.1	19.8	23.1	26.3	30.3	29.8
Breastfeeding duration (months)*						
Never or <1	45.1	56.9	61.3	65.1	69.0	73.2
week	22.6	20.1	19.0	17.7	16.6	12.4
<3	13.3	11.5	10.2	8.8	7.5	5.4
3-6	9.8	6.9	6.0	5.1	3.5	3.9
6-9	6.3	3.1	2.7	2.6	2.9	3.9
9-12	2.9	1.5	0.9	0.8	0.6	1.3
≥12						
Adult smoking status during the past year*						
Never	69.0	68.3	68.7	67.5	67.9	68.3
Past	21.7	22.4	21.0	21.8	20.9	19.7
Current	9.1	9.2	10.1	10.6	11.2	11.8

Table 3.1, cont.

Adult activity level during the past year in 1991 (Metabolic Equivalents/week)*						
<3-8	41.1	35.5	36.5	38.1	40.5	45.6
9-26	37.0	37.1	37.1	36.4	36.0	32.5
27-42+	21.9	27.4	26.4	25.7	23.5	21.9
Adult hours watching television daily during the past year (hours)						
<3	94.3	94.2	93.7	93.1	91.5	87.5
3-5.7	5.2	5.2	5.7	6.4	7.5	11.8
>5.7	0.5	0.6	0.5	0.6	1.1	0.7
			Mean (Standard Deviation)			
Maternal pre-pregnancy Body Mass Index (kg/m^2)	21.3 (2.6)	21.1 (2.3)	21.2 (2.5)	21.3 (2.6)	21.5 (2.8)	21.5 (2.8)
Paternal Body Mass Index at nurse's birth (kg/m^2)	23.4 (2.5)	23.6 (2.6)	23.6 (2.6)	23.7 (2.6)	23.7 (2.7)	23.8 (2.8)
Birthweight (lbs)	6.9 (1.2)	6.8 (1.1)	6.8 (1.1)	6.8 (1.1)	6.8 (1.1)	6.8 (1.2)
Gestational age (weeks)[3]	39.7 (2.6)	39.7 (2.6)	39.7 (2.6)	39.7 (2.6)	39.6 (2.6)	39.7 (2.6)
Age at menarche (years)	12.4 (1.4)	12.5 (1.4)	12.5 (1.4)	12.4 (1.4)	12.4 (1.4)	12.2 (1.5)
Age in adulthood (years)	38.9 (4.2)	35.2 (4.3)	34.7 (4.3)	34.2 (4.3)	33.8 (4.3)	33.7 (4.2)
Caloric intake in adulthood (kcal)	1790.4 (518.8)	1794.3 (503.1)	1804.3 (517.6)	1802.6 (525.4)	1802.3 (526.9)	1816.2 (554.3)
Alternative Healthy Eating Index score in adulthood	44.9 (10.4)	45.0 (10.5)	43.9 (10.5)	42.8 (10.3)	42.1 (10.1)	40.8 (10.0)

*P<0.05 for differences by hours watching television daily at 3-5 years

[1]8% missing [2]2% missing [3]42% missing

Television viewing at ages 3-5

Table 3.2 shows the association between hours watching TV daily at ages 3-5 and the adjusted ORs and 95% CIs for overweight/obesity at ages 5, 10, 18 and in adulthood with “no TV” as the referent group. Watching TV for ≥2 hours/day at ages 3-5 was associated with a dose-dependent higher adjusted odds of overweight/obesity at age 5: ORs and 95% CIs were 1.16 (95% CI: 1.00, 1.35) for 2 hours/day; 1.39 (95% CI: 1.15, 1.69) for 3 hours/day; and 1.61 (95% CI: 1.20, 2.17) for ≥4 hours/day. ORs of a slightly smaller magnitude were seen for TV viewing and overweight/obesity at age 10.

Watching TV for ≥4 hours daily was associated with a 1.31-fold higher odds (95% CI: 1.00, 1.70) of overweight/obesity at age 18 and 1.32-fold higher odds (95% CI: 1.10, 1.59) in adulthood in the parental and daughter covariate-adjusted models.

In sensitivity analyses, the association between TV viewing at ages 3-5 and overweight/obesity in adulthood was partially accounted for by adult TV viewing and PA (age-adjusted OR: 1.71, 95% CI: 1.44, 2.03 versus adult TV viewing and PA-adjusted OR: 1.24, 95% CI: 1.04, 1.47). TV viewing for ≥4 hours/day at ages 3-5 was associated with a 1.29-fold (95% CI: 1.07, 1.55) higher odds of overweight/obesity in adulthood after adjusting for early life overweight/obesity and age 5, 10 and adult covariates (data not shown). Of note, the spearman correlation coefficient between somatotype at age 5 and BMI in adulthood was 0.24.

Table 3.2. Adjusted Odds Ratios and 95% Confidence Intervals for Overweight/Obesity at Ages 5, 10, 18 and in Adulthood by Hours Watching Television Daily at Ages 3-5

Hours watching television daily at ages 3-5 (hours)	Age-adjusted model[a]	Model adjusted for age and physical activity at ages 3-5	Model adjusted for parental and daughter-covariates[b]
Somatotype ≥5 at age 5			
No television	Reference	Reference	Reference
0.5	0.95 (0.79, 1.14)	0.95 (0.79, 1.14)	0.96 (0.79, 1.15)
1	1.08 (0.95, 1.24)	1.08 (0.95, 1.24)	1.07 (0.93, 1.23)
2	**1.22 (1.06, 1.41)***	**1.20 (1.04, 1.39)***	**1.16 (1.00, 1.35)***
3	**1.53 (1.27, 1.85)***	**1.46 (1.21, 1.77)***	**1.39 (1.15, 1.69)***
≥4	**1.87 (1.40, 2.49)***	**1.71 (1.28, 2.29)***	**1.61 (1.20, 2.17)***
P-for-trend	**<0.001***	**<0.001***	**<0.001***
Somatotype ≥5 at age 10			
No television	Reference	Reference	Reference
0.5	0.91 (0.79, 1.04)	0.91 (0.79, 1.05)	0.94 (0.81, 1.08)
1	1.03 (0.93, 1.14)	1.03 (0.93, 1.14)	1.05 (0.94, 1.17)
2	**1.20 (1.07, 1.34)***	**1.18 (1.05, 1.32)***	**1.18 (1.05, 1.32)***
3	**1.44 (1.24, 1.67)***	**1.38 (1.19, 1.61)***	**1.35 (1.15, 1.57)***
≥4	**1.62 (1.28, 2.06)***	**1.50 (1.18, 1.91)***	**1.46 (1.14, 1.86)***
P-for-trend	**<0.001***	**<0.001***	**<0.001***
BMI ≥25kg/m^2 at age 18			
No TV	Reference	Reference	Reference
0.5	**0.84 (0.72, 0.98)***	**0.85 (0.72, 0.99)***	0.89 (0.76, 1.05)
1	0.95 (0.85, 1.07)	0.95 (0.85, 1.07)	0.98 (0.87, 1.11)
2	1.10 (0.97, 1.24)	1.08 (0.96, 1.22)	1.06 (0.94, 1.21)
3	**1.26 (1.07, 1.48)***	**1.21 (1.03, 1.42)***	1.12 (0.94, 1.33)
≥4	**1.57 (1.22, 2.01)***	**1.47 (1.14, 1.88)***	**1.31 (1.00, 1.70)***
P-for-trend	**<0.001***	**<0.001***	**0.04***
BMI ≥25kg/m^2 in adulthood			
No television	Reference	Reference	Reference
0.5	**0.88 (0.80, 0.96)***	**0.88 (0.80, 0.97)***	0.92 (0.83, 1.01)
1	0.95 (0.89, 1.02)	0.95 (0.89, 1.02)	0.96 (0.89, 1.04)
2	**1.08 (1.00, 1.16)***	**1.07 (1.00, 1.16)***	1.02 (0.94, 1.11)
3	**1.24 (1.12, 1.38)***	**1.22 (1.10, 1.36)***	1.07 (0.95, 1.19)
≥4	**1.71 (1.44, 2.03)***	**1.65 (1.39, 1.96)***	**1.32 (1.10, 1.59)***
P-for-trend	**<0.001***	**<0.001***	**0.001***

[a]Adjusted for age at daughter's questionnaire return
[b]Adjusted for:
Ages 5 and 10 (maternal education, maternal and paternal body mass index, maternal gestational weight gain, smoking during pregnancy, activity during pregnancy, home ownership, daughter's birthweight, gestational age, birth year, breastfeeding duration, physical activity at ages 3-5 and age at questionnaire return)
Age 18 (ages 5 and 10 covariates and age at menarche)
Adulthood (age 18 covariates and adult smoking status, activity level, hours watching TV daily, caloric intake and Alterative Healthy Eating Index score)

Television viewing at ages 5-10

The relation between hours watching TV daily at ages 5-10 and overweight/obesity at ages 10, 18 and in adulthood (using “no TV” as the referent group) appears in Table 3.3. Similar ORs to the ORs from TV viewing at ages 3-5 were seen in the final models for ≥4 hours versus no TV viewing daily: 1.45 (95% CI: 1.15, 1.83) at age 10, 1.39 (95% CI: 1.08, 1.80) at age 18 and 1.25 (95% CI: 1.05, 1.49) in adulthood.

Table 3.3. Adjusted Odds Ratios and 95% Confidence Intervals for Overweight/Obesity at Ages 5, 10, 18 and in Adulthood by Hours Watching Television Daily at Ages 5-10

Hours watching television daily at ages 5-10 (hours)	**Age-adjusted model[a]**	**Model adjusted for age and physical activity at ages 5-10**	**Model adjusted for parental and daughter-covariates[b]**
Somatotype ≥5 at age 10			
No television	Reference	Reference	Reference
0.5	**0.81 (0.67, 0.99)***	**0.82 (0.68, 1.00)***	0.83 (0.68, 1.02)
1	0.92 (0.79, 1.06)	0.92 (0.79, 1.07)	0.92 (0.79, 1.08)
2	1.06 (0.91, 1.23)	1.04 (0.90, 1.21)	1.02 (0.87, 1.19)
3	**1.31 (1.11, 1.55)***	**1.24 (1.04, 1.46)***	1.18 (0.99, 1.41)
≥4	**1.69 (1.36, 2.11)***	**1.50 (1.20, 1.88)***	**1.45 (1.15, 1.83)***
P-for-trend	**<0.001***	**<0.001***	**<0.001***
BMI ≥25kg/m^2 at age 18			
No television	Reference	Reference	Reference
0.5	**0.71 (0.57, 0.88)***	**0.72 (0.57, 0.90)***	**0.75 (0.60, 0.95)***
1	0.93 (0.79, 1.10)	0.94 (0.79, 1.11)	0.96 (0.81, 1.15)
2	1.06 (0.89, 1.25)	1.04 (0.88, 1.23)	1.02 (0.86, 1.22)
3	**1.35 (1.12, 1.62)***	**1.28 (1.06, 1.55)***	1.20 (0.99, 1.45)
≥4	**1.66 (1.30, 2.11)***	**1.49 (1.17, 1.90)***	**1.39 (1.08, 1.80)***
P-for-trend	**<0.001***	**<0.001***	**<0.001***
BMI ≥25kg/m^2 in adulthood			
No television	Reference	Reference	Reference
0.5	**0.84 (0.74, 0.96)***	**0.85 (0.74, 0.96)***	**0.87 (0.75, 1.00)***
1	0.93 (0.84, 1.03)	0.93 (0.84, 1.03)	0.91 (0.81, 1.01)
2	1.07 (0.97, 1.19)	1.06 (0.96, 1.18)	0.97 (0.87, 1.09)
3	**1.35 (1.20, 1.52)***	**1.31 (1.17, 1.48)***	1.10 (0.97, 1.25)
≥4	**1.64 (1.40, 1.93)***	**1.55 (1.32, 1.82)***	**1.25 (1.05, 1.49)***
P-for-trend	**<0.001***	**<0.001***	**<0.001**

[a]Adjusted for age at daughter's questionnaire return
[b]Adjusted for:
Ages 5 and 10 (maternal education, maternal and paternal body mass index, maternal gestational weight gain, smoking during pregnancy, activity during pregnancy, home ownership, daughter's birthweight, gestational age, birth year, breastfeeding duration, physical activity at ages 3-5 and age at questionnaire return)
Age 18 (ages 5 and 10 covariates and age at menarche)
Adulthood (age 18 covariates and adult smoking status, activity level, hours watching TV daily, caloric intake and Alterative Healthy Eating Index score)

Composite score (television viewing and physical activity)

Table 3.4 has the parental and daughter covariate-adjusted ORs for overweight/obesity at ages 5, 10, 18 and in adulthood by a composite score of TV viewing and PA at ages 3-5 and 5-10. Compared to daughters with low TV/high PA at ages 3-5, those with low TV/low PA, high TV/high PA and high TV/low PA had higher odds of overweight/obesity throughout life. The highest ORs were seen among those who had high TV/low PA: 3.22 (95% CI: 2.23, 4.65) at age 5, 2.80 (95% CI: 2.03, 3.86) at age 10, 2.30-fold (95% CI: 1.63, 3.26) at age 18 and 1.82 (95% CI: 1.36, 2.45) in adulthood. Similar results were seen when the composite score was assessed at ages 5-10. Daughters with high TV/low PA had the highest ORs for overweight/obesity: 4.41 (95% CI: 3.48, 5.57) at age 10, 3.91 (95% CI: 3.04, 5.02) at age 18 and 2.19 (95% CI: 1.74, 2.76) in adulthood.

Table 3.4. Adjusted Odds Ratios and 95% Confidence Intervals for Overweight/Obesity at Ages 5, 10, 18 and in Adulthood by Joint Effects of Hours Watching Television Daily and Physical Activity

Joint effects/composite score	Somatotype ≥5 at age 5[a]	Somatotype ≥5 at age 10[a]	BMI ≥25kg/m^2 at age 18[b]	BMI ≥25kg/m^2 in adulthood[c]
Ages 3-5				
No television or ≤2 hours/day and highly active/active	Reference	Reference	Reference	Reference
No television or ≤2 hours/day and mostly inactive/inactive	**2.01 (1.62, 2.49)***	**1.91 (1.60, 2.27)***	**1.84 (1.52, 2.24)***	**1.30 (1.13, 1.51)***
≥3 hours of television/day and highly active/active	**1.33 (1.14, 1.55)***	**1.29 (1.14, 1.45)***	**1.16 (1.01, 1.32)***	**1.12 (1.02, 1.23)***
≥3 hours of television/day and mostly inactive/inactive	**3.22 (2.23, 4.65)***	**2.80 (2.03, 3.86)***	**2.30 (1.63, 3.26)***	**1.82 (1.36, 2.45)***
P-for-trend	**<0.001***	**<0.001***	**<0.001***	**<0.001***
Ages 5-10				
No television or ≤2 hours/day and highly active/active	-	Reference	Reference	Reference
No television or ≤2 hours/day and mostly inactive/inactive	-	**2.51 (2.14, 2.95)***	**2.13 (1.78, 2.56)***	**1.55 (1.35, 1.79)***
≥3 hours of television/day and highly active/active	-	**1.25 (1.12, 1.38)***	**1.22 (1.09, 1.36)***	**1.19 (1.11, 1.28)***
≥3 hours of television/day and mostly inactive/inactive	-	**4.41 (3.48, 5.57)***	**3.91 (3.04, 5.02)***	**2.19 (1.74, 2.76)***
P-for-trend	-	**<0.001***	**<0.001***	**<0.001***

[a]Adjusted for maternal education, maternal and paternal body mass index, maternal gestational weight gain, smoking during pregnancy, activity during pregnancy, home ownership at nurse's birth nurse's birthweight, gestational age, birth year, breastfeeding duration and age at questionnaire return

[b]Adjusted for age 5 and 10 covariates and age at menarche

[c]Adjusted for age 18 covariates and adult smoking status, activity level, hours watching TV daily, caloric intake and Alterative Healthy Eating Index score in 1991

DISCUSSION

In this study, we examined the association between hours watching TV daily during early and late childhood and overweight/obesity throughout the life course. We report that watching TV for ≥4 hours daily at ages 3-5 and 5-10 was related to 25-61% higher odds of overweight/obesity throughout life after adjustment for parental and daughter covariates. A composite score of high daily TV viewing and low PA during childhood was associated with 82-441% higher odds of overweight/obesity across the life course. Thus, we observe a window of vulnerability for risk factors for obesity in early life with potential effects extending into later life.

Importantly, our results show that only two thirds of the association between childhood TV viewing and adult overweight/obesity is accounted for by adult TV viewing and PA. Thus the signal from TV viewing in early childhood and its association with overweight/obesity in adulthood (ages 26-45) may persevere, regardless of adult behaviors. Further, although evidence suggests that obesity may track throughout life, we found a persistent association between early life TV viewing and adult overweight/obesity, irrespective of early life overweight/obesity.

Nine percent and 15% of mothers reported their daughter watching TV for >2 hours/day at ages 3-5 and 5-10, respectively. However, even with these relatively low proportions from >50 years ago, our results suggest a need for interventions to reduce screen time among youth. This is especially important in the current era of ever-expanding time to be “in front of screens” with nationally representative statistics indicating between 58-79% of children engaging in screen time for >2 hours/day.[42,93] The persistent effects of childhood TV viewing on overweight/obesity later in life, particularly in late adolescence and adulthood, are modest in our study and others.[59,60] However, given the widespread use of a variety of screen media among infants and children today,[107] these associations may translate into large effect sizes at the population level. In contrast, the strength of the independent and joint effects of TV viewing and PA in our study are relatively large, in comparison to other modifiable risk factors for obesity in early life.[113] This suggests that TV viewing and PA are targets for public health interventions to tackle the overweight/obesity epidemic throughout life.

Our results are in accord with several studies. Using nationally representative longitudinal data from a more recent cohort (born 1970's), each additional hour spent watching TV on the weekend at age 5 was associated with 7% higher odds of obesity at age 30 (adjusted OR: 1.07, 95% CI: 1.01, 1.13).[60] In a prospective cohort of preschool aged children in 1987, those watching TV for ≥3 hours versus <1.75 hours/day had the greatest increases in mean BMI and body fat from 4 to 11 years.[22] In a prospective cohort study of adolescents followed from 1995-2001,[23] a lower odds of obesity appeared in adulthood for adolescent screen time of 4 versus 40 hours/week, with stronger associations seen among females (OR: 0.58, 95% CI: 0.43, 0.80) than males (OR: 0.78, 95% CI: 0.61, 0.99). The same study found that a profile of high screen time and low moderate-to-vigorous physical activity bouts was associated with higher proportions of obesity than a profile of low screen time and high moderate-to-vigorous physical activity bouts.

Interestingly, we report that 0.5 hours of TV/day at ages 5-10 was associated with reduced odds of overweight/obesity at age 18 and in adulthood. These findings may indicate that daughters who watched minimal TV/day may have generally healthier lifestyles, comparable to those with no TV viewing. However, we do not have sufficient data on childhood diet, sleep habits or activities replacing TV viewing to decipher this finding. It is also possible that this result may be due to chance or that mothers may have been inclined to report a low estimate of TV viewing, rather than no TV, if her daughter watched very minimal amounts of TV.

Several mechanisms have been postulated in the literature to explain the association between long hours of TV viewing and overweight/obesity. Time spent in front of the TV is time spent being sedentary with potentially less energy expenditure via displacement of time spent being physically active.[45,46] Research indicates that children have higher energy intake[114] and consume more meals and snacks,[103] sugar-sweetened beverages, high fat diets, and less fruits and vegetables during TV viewing.[115] Exposure to food advertisements with TV viewing influences foods children request.[116] Children aged 2-11 years in the United States today watch approximately 12 food-related advertisements/day;[117] 86% of advertisements promote foods high in saturated fat, sugar and sodium.[118] Other proposed mechanisms include the hypometabolic effect of watching TV;[119] impaired sleep quality;[120,121] distraction from habitual food intake control or satiety and satisfaction cues; conditioning of food consumption; interference with memory formation and regulation[122] and fewer family meals[123]. Future research might explore the mediating effects of these potential mechanisms on the relationship between screen time and obesity.

Our study has strengths and limitations. Among the strengths, we analyzed a large cohort with adjustment for important confounders associated with obesity. Our exposure data were obtained from the mothers independent of and at a different time than the outcome from the daughters. Additionally, we have data on both childhood and adult TV and PA, but not at age 18. Among the limitations, data on childhood TV viewing and PA may be subject to recall bias, given that mothers were asked to recall the exposure decades after it occurred (approximately 32-52 years later). TVs were relatively new during the birth years of the daughters which may have made recall slightly more accurate. However, the length of time between occurrence and reporting of the exposure likely introduced measurement error. We expect that any misclassification is non-differential and thus likely biased associations towards the null. The study is limited by lack of generalizability due to the homogeneous ethnic sample (97% Caucasian white). We were unable to determine if one sex was more negatively affected by screen time than the other[23,102,103] since our sample has females only. Information on PA of the daughters during childhood may be based on maternal perception – i.e. we do not know whether a "highly active" daughter was active due to involvement in scheduled PA or unsupervised PA and whether these could result in differential outcomes. Daughter's recalled somatotype in childhood, weight at age 18 and current weight and height in adulthood may be subject to self-report bias; however, these measures have been validated in previous studies.[72-74,77,78] Given the differences in measurements to assess overweight/obesity in childhood versus adulthood, it is unclear whether daughters who were overweight/obese in childhood were also overweight/obese in adulthood. Thus, it is possible that the association between early life TV viewing and obesity is due to tracking of overweight/obesity, or due to amount of childhood TV viewing. Lastly, although dietary data was collected at ages 3-5 in a semi-quantitative food frequency questionnaire, the questionnaire has not been validated in this population and the foods listed do not comprehensively represent a child's diet at ages 3-5. Poor correlation was reported between records and maternal recall of preschool diet an average of 43 years later in a comparable cohort.[124] We therefore did not adjust for childhood diet in our analyses. No dietary data was collected at age 18 and although we saw a decreasing mean Alterative Healthy Eating Index score in adulthood with increasing hours of daily childhood TV viewing, adult dietary data were collected simultaneously with data on overweight/obesity in adulthood. This may lead to an underestimation of associations due to reporting of socially desirable answers and/or reverse causation.

CONCLUSIONS

In conclusion, our results suggest that long hours of TV viewing (≥4 hours/day) in childhood are associated with higher odds of overweight/obesity throughout life; the association is stronger when combined with low PA. Therefore, there is a need for a) interventions to reduce TV viewing among youth; and b) incorporation of PA as part of interventions, given that low TV viewing may not translate into high PA.[48] Future research is needed to replicate our findings.

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Chapter 4: Television Viewing during Childhood and Change in Anthropometry from Childhood to Early Adolescence

ABSTRACT

This study examines the association between television (TV) viewing during childhood and anthropometric trajectories from childhood through adolescence. Among 613 mother-offspring dyads in a nested case-control study with follow-up, each mother reported TV viewing of her child at 3-6 years, weight/height were abstracted from medical records at 4 years, and weight, height and waist circumference (WC) were measured at 10.8 (girls)/11.8 (boys) and 12.8 years (both). Linear mixed models were computed to estimate the effect of childhood TV viewing on body mass index (BMI) and weight Z-score trajectories from childhood to adolescence. Multiple linear regression analyses were used to examine WC and waist-to-height ratio Z-scores in early adolescence by childhood TV. Watching ≥2 versus ≤0.5 hours of TV/day at 3-6 years was associated with a 0.04-unit higher BMI Z-score from 4 to 12.8 years. TV viewing was not related to change in weight Z-score from 4 to 12.8 years and to WC and waist-to-height ratio Z-scores at 10.8/11.8 and 12.8 years. In conclusion, two plus hours of TV viewing/day during childhood was associated with a higher BMI but not weight trajectory from childhood through adolescence. TV viewing was not related to WC and waist-to-height ratio Z-scores in adolescence.

Keywords: television viewing, childhood, body mass index, weight, trajectory

INTRODUCTION

Obesity is a worldwide epidemic with an evident rightward shift in body mass index (BMI) distributions in recent decades.[125] Research suggests that BMI trajectories are established in childhood[126] and often persist across the life course.[127,128] Investigating early life factors leading to the development and continuity of obesity may identify strategies to reverse this condition.

Sedentary behavior such as screen time may be driving the prevalence of unhealthy weight status in children and adolescents.[129,130] Screen time is omnipresent in children's environments, with global statistics indicating that approximately 54% of children aged 9-11 experience longer screen time than the guidelines of ≤2 hours/day.[131]

Research has linked screen time to obesity in some cross-sectional and longitudinal studies,[105,132] but not in others.[105] Much of this research has focused on incidence of obesity, with few studies assessing changes in anthropometric measurements over time.[133,134] Yet BMI and weight trajectories that vary by level of exposure may help identify target populations for intervention.[135,136] Limited research has assessed effect of television (TV) viewing or sedentary behavior on change in repeated measures of body size or composition longitudinally with inconsistent conclusions.[62,63,133,134] Further, few studies have examined the association between screen time and waist circumference and/or waist-to-height ratio,[63,137] both of which are better predictors of abdominal obesity and are more strongly associated with cardiometabolic risk factors than BMI.[63,138] As such, additional research is needed to examine the influence of screen time on anthropometric trajectories and a variety of body composition measurements through the life course.

TV viewing accounts for the longest duration of screen time among youth,[139] is more amenable to intervention than “sitting time,” which may be influenced by factors such as time spent in classes, and is more consistently associated with obesity than general “sedentary behavior.”[105] Thus, we examined TV viewing in early childhood as a measure of screen time in our study to assess change in BMI and weight Z-scores from childhood through adolescence; and examine the effect of TV viewing in early childhood on waist circumference (WC) and waist-to-height ratio Z-scores at 10.8/11.8 and 12.8 years with adjustment for potential confounders including intake of selected foods in childhood.

MATERIALS AND METHODS

Study Population

Among a population-based birth cohort delivered at Stavanger hospital in Norway between January 1993 and December 1995 (N=12,804), offspring of pre-eclamptic pregnancies (n=366) were identified from the Medical Birth Registry as previously described.[140] Briefly, pre-eclampsia was diagnosed in pregnant women using information from clinical charts and based on gestation age, diastolic blood pressure and proteinuria levels in accordance with criteria from the Collaborative Low-dose Aspirin Study in Pregnancy group.[141] Two normotensive pregnancy controls (n=659) who delivered at the same hospital were matched to each pre-eclamptic pregnancy case; one offspring birth date and sex match and one maternal age match, forming a nested-case control study with follow-up through puberty. All offspring were invited to a follow-up study at 10.8 years in girls and 11.8 years in boys (coinciding with pubertal onset) and at 12.8 years in both (coinciding with menarche onset in girls).[142,143] An informed consent/assent form was signed by participating mothers and their children at follow-up. A total of 614 and 468 children assented at the first and second follow-ups, respectively. The Norwegian Data Inspectorate, the Regional Committee for Ethics in Medical Research Western Norway and the Institutional Review Boards of the National Cancer Institute and the University of Texas at Austin approved the study.[144]

Television viewing during childhood

At the first follow-up (10.8/11.8 years), mothers completed a questionnaire about their pregnancy and early life exposures of the index child, including TV viewing. Specifically, mothers were asked to recall the child's TV viewing at ages 3-6 years with the following response categories: "No TV," "up to 0.5 hours/day," "1 hour/day," "2 hours/day," "3 hours/day," "4 hours/day," or "5 or more hours/day." Categories were combined as follows due to the limited number of responses at the lower and upper end: "≤0.5 hours/day," "1 hour/day" and "≥2 hours/day."

Childhood diet

From the questionnaire at the first follow-up, mothers reported the frequency of intake of average portion sizes of 36 foods by the child at ages 3-6 years. This semiquantitative food frequency questionnaire included a variety of dairy products, fruits and fruit juices, vegetables, meats and carbohydrate-rich foods. Frequency of intake categories were combined when responses were low.

Anthropometric assessments: body mass index, weight, waist circumference and waist-to-height ratio

Birthweight was abstracted from hospital records and weight and height measurements were abstracted from clinical records of routine well-baby visits at 4 years of age. Measurements from the closest visit were substituted if values were missing for the target visit at age 4 and calculations were based on the exact age for the visit when the measurement was taken. At the first and second follow-ups, weight, height and WC were measured twice in the offspring by trained nurses to calculate the mean measurement for the analysis.[140] BMI was calculated from weight and height and waist-to-height ratio was calculated from WC and height. Z-scores for weight, BMI, WC and waist-to-height ratio were calculated by age and sex of the child based on the Norwegian growth reference.[145,146]

Potential Confounders

Measures of obesity such as BMI, weight and WC that are related to genetic and lifestyle factors were assessed as potential confounders in the models (*a priori*) from medical birth registries: maternal pre-eclampsia status (not pre-eclamptic, mild/moderate pre-eclampsia, severe preeclampsia), age at child's birth (years), and child's birthweight (Z-score), gestational age at birth (weeks), delivery by caesarian section (yes, no) and sex (male, female). Maternal gestational weight gain (<7, 7-10, 10-15, 15-20, >20 kg), and education level at delivery (<9, 9-12, >12 years), and child's birth order (first born, not first born), breastfeeding duration (<3, 3-6, 6-9, 9-12, >12 months) and physical activity at 3-6 years (high, normal, low) were obtained from the maternal questionnaire at the first follow-up. Maternal BMI was calculated as kg/m^2 using weight from first trimester health care visit and height from the first follow-up.

Statistical Analyses

Demographic and lifestyle characteristics of the mother-child dyads were compared with means ± standard deviations (SD) for continuous variables and frequencies and percentages for categorical variables by hours spent watching TV per day at 3-6 years. To test for differences in means across TV viewing categories, one-way ANOVA and Kruskal-Wallis test for parametric and non-parametric variables, respectively, were computed. Chi-square tests were used to compare frequencies in categorical variables, including frequency of food intake, by hours of TV viewing per day at 3-6 years. A principal component analysis was computed on the 36 food items, and four factors accounting for approximately 30% of the variance were extracted and entered as confounders into models.

Linear mixed models (proc mixed) were computed to analyze the association between TV viewing at 3-6 years and change in Z-scores for BMI and weight from 4 to 12.8 years following adjustment for the aforementioned potential confounders. An unstructured covariance matrix was used and random intercepts and age slopes were included to account for correlations between repeated measures (i.e. within each child). An age by TV viewing interaction was included to determine whether change in BMI and weight Z-scores from 4 to 12.8 years differed by level of TV viewing. This model is robust to missing data from participants who did not assent to the two follow-ups, and irregularly spaced occasions for measurement.[147] The estimated coefficients (β), 95% confidence intervals (CI) and P-values for parameter estimates are reported.

Next, linear regression models (general linear model: GLM) were computed to assess the crude association between TV viewing at 3-6 years and the Z-scores for WC and waist-to-height ratio at 10.8/11.8 and 12.8 years before and after adjustment for confounders and further analysis by sex. The estimated coefficients (β), 95% confidence interval (CI) and F-test with P-values are reported. The linear mixed model analysis was computed using SAS 9.4 (SAS Institute Inc., Cary, NC) and the GLM analysis using IBM SPSS for Windows (version 24, Chicago, IL, USA).

RESULTS

Characteristics of the mother-child dyads by TV viewing per day at 3-6 years are presented in Table 4.1. Thirty-six percent of children watched ≤0.5 hours of TV/day, 50% watched 1 hour/day and 14% watched ≥2 hours/day. Thirty-five percent of mothers had pre-eclampsia and 36% gained 10-15 kg during pregnancy; 51% had 9-12 years of education. The mean maternal BMI at the first antenatal visit was 23.6 ± 3.8 kg/m^2 and the average maternal age at child's birth was 27.9 ± 4.8 years. Approximately 50% of children were boys, 47% were first-born and 14% were delivered via caesarian section. The mean Z-score for birthweight was -0.15 ± 1.2, the average gestational age at birth was 39.2 ± 2.6 weeks and 73% of children were breastfed for >6 months. The mean Z-scores for BMI and weight at 4 years were -0.03 ± 1.1 and 0.06 ± 1.1, respectively. Sixty-two percent of children were active at 3-6 years. At 10.8/11.8 years, the mean Z-score was: -0.13 ± 1.2 for BMI; -0.01 ± 1.1 for weight; 0.14 ± 1.1 for WC; and 0.12 ± 1.1 for waist-to-height ratio. At 12.8 years, the mean Z-score was: -0.10 ± 1.2 for BMI; -0.01 ± 1.1 for weight; 0.43 ± 1.0 for WC; and 0.44 ± 1.0 for waist-to-height ratio. Maternal gestational weight gain and age, and child's breastfeeding duration, waist-to-height ratio Z-score at 10.8/11.8 years and BMI Z-score at 12.8 years significantly differed by hours of TV viewing/day at 3-6 years ($P<0.05$).

Frequency of intake of ice cream, peanut butter, mayonnaise, spinach, hot dogs/sausage, foods from minced meat, fish and seafood, pasta, bread, cookies/donuts/cakes, cereal, fried potato and other potato varied significantly ($P<0.05$) by categories of TV viewing per day at 3-6 years (Table 4.2). A higher proportion of children who watched ≥2 hours of TV/day ate more ice cream, peanut butter, mayonnaise, hot dogs/sausage, foods from minced meat, pasta, cookies/donuts/cakes, cereal, fried potato and other potato than those with <2 hours/day. In contrast, a higher proportion of children who watched ≥2 hours of TV/day ate spinach, bread, and fish and seafood less than those watching TV for <2 hours/day.

Table 4.1. Demographic and Lifestyle Characteristics of the Mother-Child Dyads (n=613)

	TV viewing at 3-6 years		
	≤0.5 hours TV/day (n=220)	**1 hour TV/day (n=305)**	**≥2 hours TV/day (n=88)**
Maternal characteristics			
Pre-eclampsia status, n (%)			
Not pre-eclamptic	141 (64.7)	190 (63.3)	53 (63.1)
Mild/moderate	59 (27.1)	79 (26.3)	26 (31.0)
Severe	18 (8.3)	31 (10.3)	5 (6.0)
Maternal BMI at first antenatal visit, kg/m^2, x̄ ± SD	23.7 ± 4.0	23.6 ± 3.6	23.7 ± 4.0
Maternal gestational weight gain, kg, n (%)*			
<7	23 (10.5)	14 (4.7)	6 (7.4)
7-10	34 (15.5)	43 (14.6)	10 (12.3)
10-15	84 (38.4)	102 (34.6)	27 (33.3)
15-20	33 (15.1)	76 (25.8)	13 (16)
>20	45 (20.5)	60 (20.3)	25 (30.9)
Maternal education, years, n (%)			
<9	57 (26.3)	60 (20)	16 (18.4)
9-12	95 (43.8)	161 (53.7)	51 (58.6)
>12	65 (30.0)	79 (26.3)	20 (23)
Maternal age, years, x̄ ± SD$^+$	28.7 ± 4.9	27.8 ± 4.5	27.4 ± 4.8
Child characteristics			
Male Sex, n (%)	96 (43.6)	156 (51.1)	40 (45.5)
First born, n (%)	100 (48.3)	136 (46.9)	38 (45.8)
Caesarian section delivery, n (%)	34 (15.5)	39 (13)	8 (9.6)
Birthweight, **kg**	3.4 ± 0.7	3.4 ± 0.7	3.4 ± 0.8
Birthweight, Z-score	-0.20 ± 1.3	-0.21 ± 1.2	-0.11 ± 1.3
Gestational age at birth, **weeks,** x̄ ± SD	39.3 ± 2.4	39.2 ± 2.6	39.4 ± 2.8
Duration of breastfeeding, **months**,			
n (%)*	25 (12.4)	37 (13.3)	17 (21.0)
<3	17 (8.4)	42 (15.1)	14 (17.3)
3-6	39 (19.3)	65 (23.4)	24 (29.6)
6-9	58 (28.7)	81 (29.1)	16 (19.8)
9-12	63 (31.2)	53 (19.1)	10 (12.3)
>12			

Table 4.1, cont.

BMI at 4 years, kg/m^2 **BMI at 4 years**, **Z-score**	15.9 ± 1.3 -0.06 ± 1.0	16.0 ± 1.4 0.01 ± 1.1	16.0 ± 1.8 -0.009 ± 1.3
Weight at 4 years, kg **Weight at 4 years, Z-score**	17.1 ± 3.1 0.02 ± 1.0	17.4 ± 3.2 0.07 ± 1.1	17.5 ± 3.4 0.14 ± 1.0
Physical activity level at 3-6 years, n (%) Low Normal High	 22 (10.1) 133 (61.3) 62 (28.6)	 36 (12.1) 182 (61.3) 79 (26.6)	 14 (15.9) 56 (63.6) 18 (20.5)
BMI at 10.8/11.8 years, kg/m^2 **BMI at 10.8/11.8 years**, **Z-score**	17.6 ± 2.6 -0.24 ± 1.1	18.1 ± 3.1 -0.09 ± 1.2	18.3 ± 2.9 0.04 ± 1.2
Weight at 10.8/11.8 years, kg, **Weight at 10.8/11.8 years**, **Z-score**	39.2 ± 8.1 -0.10 ± 1.1	40.6 ± 9.2 0.02 ± 1.1	40.8 ± 8.8 0.09 ± 1.1
Waist circumference at 10.8/11.8 years, cm **Waist circumference at 10.8/11.8 years, Z-score**	62.3 ± 6.9 0.004 ± 1.1	64.0 ± 8.3 0.18 ± 1.1	64.4 ± 7.8 0.31 ± 1.0
Waist-to-height ratio at 10.8/11.8 years$^+$ **Waist-to-height ratio at 10.8/11.8 years Z-score**	0.42 ± 0.04 -0.02 ± 1.0	0.43 ± 0.05 0.17 ± 1.1	0.43 ± 0.05 0.33 ± 1.1
BMI at 12.8 years, kg/m^{2‡} **BMI at 12.8 years**, **Z-score**	18.4 ± 2.8 -0.28 ± 1.2	18.9 ± 3.1 -0.06 ± 1.2	19.4 ± 2.7 0.15 ± 1.0
Weight at 12.8 years, kg, **Weight at 12.8 years**, **Z-score**	46.6 ± 9.4 -0.14 ± 1.1	47.9 ± 9.6 0.01 ± 1.1	49.2 ± 8.9 0.21 ± 0.98
Waist circumference at 12.8 years, cm, **Waist circumference at 12.8 years**, **Z-score**	67.4 ± 7.4 0.37 ± 0.97	68.3 ± 8.0 0.42 ± 1.1	69.2 ± 7.6 0.61 ± 0.89
Waist-to-height ratio at 12.8 years **Waist-to-height ratio at 12.8 years, Z-score**	0.43 ± 0.05 0.36 ± 0.92	0.43 ± 0.05 0.45 ± 1.1	0.43 ± 0.04 0.58 ± 0.96

All anthropometric measurements at birth and ages 4, 10.8/11.8 and 12.8 are presented as $\bar{x} \pm SD$

[1]P<0.05 for differences by television viewing at 3-6 years using Chi-square tests

[2]P<0.05 for differences by television viewing at 3-6 years using Kruskal-Wallis tests

[3]P<0.05 for differences by television viewing at 3-6 years using one-way ANOVA

Table 4.2. Frequency of Consumption of Foods at 3-6 Years by Television Viewing at 3-6 Years

	≤0.5 hours/day (n=220)	**1 hour/day (n=305)**	**≥2 hours/day (n=88)**
	%		
Milk			
Never or 1-3 glasses/month	4.1	3.0	2.3
1-6 glasses /week	5.9	5.4	5.6
1 glass/day	17.8	18.6	17.9
2-3 glasses/day	66.2	67.6	61.2
≥4 glasses/day	5.9	5.4	6.0
Ice cream*			
Never or 1-3 times/month	78.8	71.4	56.3
1 time/week	18.4	23.9	33.3
≥2 times/week	2.8	4.7	10.3
Margarine			
Never	33.6	30.6	31.2
1-3 pats/month	5.6	5.8	5.4
1 pat/week	6.1	4.1	4.9
2-6 pats/week	5.1	6.5	6.1
1 pat/day	7.9	14.8	11.4
≥2 pats/day	41.6	38.1	41.0
Butter			
Never	37.1	36.6	36.7
1-3 pats/month	9.4	6.3	8.2
1 pat/week	4.2	3.5	3.8
2-6 pats/week	4.7	6.0	3.5
1 pat/day	5.2	7.7	7.0
≥2 pats/day	39.4	39.8	38.4
Peanut butter*			
Never	87.4	83.2	75.0
1-3 pats/month	10.3	10.8	15.9
≥1 pats/week	2.3	6.1	9.1
Mayonnaise*			
Never	68.5	62.0	57.5
1-3 pats/month	16.4	13.5	11.5
1 pat/week	5.5	9.4	16.1
≥2 pats/week	9.6	15.2	14.9
Apples			
Never or 1-3/month	7.3	5.1	9.1
1 time/week	13.7	14.5	15.1
2-4 times/week	55.7	58.8	56.6
5-6 times/week	13.7	14.2	13.6
≥1/day	9.6	7.4	8.3
Bananas			
Never or 1-3/month	8.2	10.3	15.9
1/week	21.6	22.1	18.3
2-4/week	57.2	59.1	61.0
≥5/week	13.0	8.5	4.9

Table 4.2, cont.

Raisins			
Never	30.0	31.5	38.6
1-3 times/month	36.4	39.3	31.8
1 time/week	24.0	20.0	20.5
≥2 times/week	9.7	9.2	9.1
Oranges			
Never	17.8	16.4	20.7
1-3/month	42.5	41.6	33.3
1/week	22.8	23.5	24.1
≥2/week	16.9	18.4	21.8
Orange juice			
Never	32.4	31.3	28.7
1-3 glasses/month	33.3	36.0	26.4
1-3 glasses/week	25.1	23.6	31.0
≥1 glass/day	9.1	9.1	13.8
Apple juice			
Never	20.5	14.9	17.2
1-3 glasses/month	40.0	41.0	34.5
1-3 glasses/week	27.0	28.5	28.7
≥1 glass/day	12.6	15.6	19.5
Broccoli			
Never	33.2	38.7	44.3
1-3 times/month	26.7	25.6	23.9
1 time/week	21.7	20.9	17.0
≥2 times/week	18.4	14.8	14.8
Carrots			
Never or 1-3 times/month	10.6	15.9	17.0
1 time/week	13.0	18.0	14.8
2-4 times/week	55.1	51.2	54.5
≥5 times/week	21.3	14.9	13.6
Green beans			
Never	93.6	94.6	90.9
≥1 time/month	6.4	5.4	9.1
Peas			
Never	61.2	57.9	55.8
1-3 times/month	26.9	28.6	32.6
1 time/week	5.9	7.7	5.8
≥2 times/week	5.9	5.7	5.8
Corn			
Never	34.2	37.4	32.2
1-3 times/month	31.1	32.7	34.5
1 time/week	25.6	17.5	14.9
2 times/week	9.1	12.5	18.4
Spinach*			
Never	94.1	96.3	86.4
≥1 times/month	5.9	3.7	13.6

Table 4.2, cont.

Eggs			
Never	11.0	14.9	14.8
1-3 eggs/month	37.6	34.9	31.8
1 egg/week	39.9	41.0	35.2
≥2 eggs/week	11.5	9.2	18.2
Hot dogs/sausage*			
Never or 1-3 times/month	50.9	34.4	27.3
1 time/week	40.8	57.0	55.7
≥2 times/week	8.3	8.6	17.0
Meats on bread			
Never	6.0	5.8	6.9
1-3 times/month	13.4	9.5	6.9
1 time/week	17.5	18.7	18.4
2-4 times/week	50.2	48.6	50.6
≥5 times/week	12.9	17.3	17.2
Food from minced meat*			
Never or 1-3 times/month	18.4	9.5	11.4
1 time/week	51.2	52.7	44.3
≥2 times/week	30.4	37.8	44.3
Pork, cattle, lamb beef			
Never or 1-3 times/month	34.9	31.2	26.1
1 time/week	47.9	51.5	51.1
≥2 times/week	17.2	17.3	22.7
Chicken, turkey			
Never or 1-3 times/month	75.4	71.7	77.3
≥1 times/week	24.6	28.3	22.7
Fish and seafood*			
Never or 1-3 times/month	24.3	24.9	30.7
1 time/week	39.0	49.5	47.7
≥2 times/week	36.7	25.6	21.6
Liver			
Never	80.3	77.2	78.8
1-3 times/month	14.7	18.0	13.6
≥1 time/week	5.0	4.8	5.7
Tomato and pasta sauce			
Never	8.2	8.5	8.0
1-3 times/month	46.1	39.6	39.1
1 time/week	39.3	43.7	41.4
≥2 times/week	6.4	8.2	11.5
Pizza			
Never	4.1	3.4	3.4
1-3 times/month	66.2	63.6	60.2
≥1 times/week	28.3	32.7	35.2
Pasta*			
Never	4.6	4.4	8.0
1-3 times/month	35.3	34.1	18.2
1 time/week	51.4	48.8	54.5
2-4 times/week	8.7	12.6	19.3

Table 4.2, cont.

Bread*			
Never to 7 slices/week	1.4	4.1	9.1
2-3 slices/day	7.4	5.6	15.9
≥4 slices/day	91.2	90.3	75.0
Cookies, donuts, cakes*			
Never or 1-3 times/month	21.6	22.8	16.3
1 time/week	51.8	46.6	38.4
≥2 times/week	26.6	30.7	45.3
Rice			
Never	4.6	6.1	4.5
1-3 times/month	34.4	29.8	25.0
1 time/week	44.5	47.1	40.9
≥2 times/week	16.5	16.9	29.5
Cereal*			
Never	32.1	22.3	21.6
1-3 bowls/month	28.4	22.9	26.1
1 bowl/week	16.1	22.9	15.9
≥2 bowls/week	23.4	31.8	36.4
Boiled potato			
Never or 1-3 times/month	3.7	3.4	2.3
1 time/week	9.1	7.0	5.7
2-4 times/week	60.3	70.5	66.7
≥5 times/week	26.9	19.1	25.3
Fried potato*			
Seldom	51.3	42.0	32.1
1-3 times/month	45.5	50.7	52.4
≥1 times/week	3.1	7.3	15.5
Other potato*			
Never	12.6	4.1	5.7
1-3 times/month	62.6	59.3	39.8
≥1 times/week	24.8	36.6	54.5

*P<0.05 for differences by television viewing at 3-6 years using Chi-Square test

In the linear mixed model (Table 4.3), an interaction between age and TVviewing indicated that children who watched ≥2 hours of TV/day versus ≤0.5 hours/day, had, on average, a higher BMI Z-score from 4 to 12.8 years (β=0.04, 95% CI=0.001, 0.08). However, no association appeared between TV viewing and weight trajectory from 4 to 12.8 years.

TV viewing was associated with WC and waist-to-height ratio at 10.8/11.8 years in crude models (Table 4.4). Specifically, TV viewing for ≥2 hours/day versus ≤0.5 hours/day was positively associated with Z-scores for WC (β=0.30, 95% CI: 0.03, 0.57) and waist-to-height ratio (β=0.34, 95% CI: 0.07, 0.62) at 10.8/11.8 years. In multiple linear regression models, after adjustment for confounders, TV viewing was no longer associated with anthropometric measurements in adolescence. When regression models were stratified by sex, no significant associations appeared (data not shown).

Table 2. Change in Z-scores for BMI and weight from 4 to 12.8 years by television viewing at 3-6 years in Norwegian children

	Outcome Variables					
	BMI Z-score			Weight Z-score		
Explanatory Variables	β	95% CI	P-value	β	95% CI	P-value
Television viewing						
1 vs 0.5 hours/day	0.001	-0.31, 0.31	0.99	0.008	-0.20, 0.21	0.94
≥2 vs 0.5 hours/day	-0.25	-0.71, 0.20	0.27	-0.11	-0.41, 0.19	0.47
Age	-0.03	-0.05, -0.006	**0.01***	-0.01	-0.03, 0.002	0.09
Television viewing*age						
1 vs 0.5 hours*age	0.02	-0.01, 0.04	0.28	0.01	-0.009, 0.03	0.29
2 vs 0.5 hours*age	0.04	0.001, 0.08	**0.04***	0.03	-0.003, 0.05	0.07
Maternal pre-eclampsia						
Mild/moderate vs none	0.16	-0.07, 0.38	0.18	0.11	-0.04, 0.26	0.14
Severe vs none	0.23	-0.16, 0.61	0.25	0.13	-0.12, 0.39	0.31
Maternal BMI	0.07	0.04, 0.09	**<0.001***	0.04	0.03, 0.06	**<0.001***
Maternal gestational weight gain						
7-10 vs <7 kg	0.04	-0.39, 0.47	0.84	-0.007	-0.29, 0.28	0.96
10-15 vs <7 kg	-0.03	-0.43, 0.37	0.88	-0.04	-0.30, 0.23	0.78
15-20 vs <7 kg	0.03	-0.39, 0.46	0.88	0.02	-0.26, 0.30	0.91
>20 vs <7 kg	0.17	-0.27, 0.61	0.44	0.08	-0.22, 0.37	0.61
Maternal education						
<9 vs >12 years	-0.05	-0.31, 0.20	0.68	-0.02	-0.19, 0.15	0.84
9-12 vs >12 years	0.03	-0.19, 0.25	0.78	0.03	-0.11, 0.18	0.65
Maternal age	-0.003	-0.03, 0.02	0.77	-0.005	-0.02, 0.01	0.52
Sex						
Male vs female	0.03	-0.15, 0.21	0.77	0.05	-0.07, 0.17	0.40
Gestational age (weeks)	0.03	-0.02, 0.07	0.34	0.01	-0.02, 0.04	0.42
Birthweight (Z-score)	0.14	0.06, 0.22	**<0.001***	0.09	0.04, 0.15	**0.001***
Birth order						
First born vs not	0.02	-0.19, 0.22	0.87	0.02	-0.11, 0.16	0.74
Caesarian section delivery						
Yes vs no	0.03	-0.31, 0.37	0.86	-0.004	-0.23, 0.22	0.97
Breastfeeding duration						
3-6 vs <3 months	0.005	-0.33, 0.34	0.98	0.006	-0.22, 0.23	0.96
6-9 vs <3 months	0.06	0.24, 0.36	0.70	0.05	-0.15, 0.25	0.63
9-12 vs <3 months	-0.07	-0.37, 0.22	0.64	-0.03	-0.22, 0.17	0.79
>12 vs <3 months	0.10	-0.21, 0.41	0.53	0.07	-0.14, 0.28	0.51
Physical activity at 3-6 years						
Low vs high	0.09	-0.23, 0.41	0.59	0.07	-0.14, 0.29	0.49
Normal vs high	0.23	0.01, 0.45	**0.04***	0.16	0.01, 0.30	**0.03***
Height (Z-score)	-	-	-	0.62	0.58, 0.67	**<0.001***
Diet factor score 1: carbohydrate rich foods (e.g. pasta, rice, pizza)	0.01	-0.08, 0.10	0.82	0.005	-0.05, 0.06	0.87
Diet Factor score 2: vegetables (e.g. corn, broccoli, peas)	0.08	-0.01, 0.17	0.08	0.05	-0.01, 0.11	0.11
Diet Factor score 3: fruits (e.g. apples, bananas, oranges)	-0.01	-0.10, 0.08	0.84	-0.01	-0.07, 0.05	0.74
Diet Factor score 4: junk foods (e.g. ice cream, bakery products)	-0.03	-0.12, 0.06	0.55	-0.02	-0.08, 0.04	0.55
Intercept	-2.52	-4.63, -0.41	**0.02***	-1.59	-3.00, -0.18	**0.03***

*P<0.05; BMI= body mass index; Z-score = standard deviations from the mean; CI= confidence interval; Age = exact ages at which measurements were taken from 4 to 12.8 years; P-value= Pr > |t|

Table 4.4. Waist Circumference and Waist-to-Height Ratio Z-scores at 10.8/11.8 and 12.8 Years among Norwegian Children by Television Viewing at 3-6 Years

Television Viewing at 3-6 years (hours/day)	**Crude Model**			**Covariate-adjusted model[a]**		
	β	95% CI	F-test P	β	95% CI	F-test P
Waist circumference Z-score at 10.8/11.8 years[a,b]						
≤0.5	0.00	0.00, 0.00		0.00	0.00, 0.00	
1	0.18	-0.14, 0.37	**0.05***	0.20	-0.01, 0.42	0.11
≥2	0.30	0.03, 0.57		0.29	-0.03, 0.62	
Waist-to-height ratio Z-score at 10.8/11.8 years[a,b]						
≤0.5	0.00	0.00, 0.00		0.00	0.00, 0.00	
1	0.18	-0.01, 0.38	**0.03***	0.13	-0.09, 0.35	0.16
≥2	0.34	0.07, 0.62		0.31	-0.02, 0.64	
Waist circumference Z-score at 12.8 years[a]						
≤0.5	0.00	0.00, 0.00		0.00	0.00, 0.00	
1	0.05	-0.15, 0.26	0.29	0.10	-0.14, 0.34	0.45
≥2	0.24	-0.06, 0.53		0.23	-0.14, 0.60	
Waist-to-height ratio Z-score at 12.8 years[a]						
≤0.5	0.00	0.00, 0.00		0.00	0.00, 0.00	
1	0.09	-0.11, 0.29	0.33	0.06	-0.17, 0.30	0.73
≥2	0.22	-0.08, 0.51		0.14	-0.22, 0.50	

[a]Adjusted for maternal pre-eclampsia, BMI, gestational weight gain, education, age, child's sex, gestational age, birthweight Z-score, birth order, caesarian section delivery, breastfeeding duration, physical activity at 3-6 years and diet factor scores (carbohydrate rich foods, vegetables, fruits, junk food)
*P<0.05; BMI= body mass index; Z-score = standard deviations from the mean; CI= confidence interval; P-value= F-test P
[b]10.8 years in girls and 11.8 years in boys

DISCUSSION

In this study of mother-offspring dyads from Norway, we examined the effect of TV viewing at 3-6 years on BMI and weight Z-score trajectories from childhood through adolescence, and assessed whether TV viewing was a predictor of WC and waist-to-height ratio Z-scores in adolescence. TV viewing for ≥2 hours/day versus ≤0.5 hours/day was associated with a higher BMI Z-score trajectory from 4 to 12.8 years, but not weight Z-score trajectory or Z-scores for WC and waist-to-height ratio at 10.8/11.8 and 12.8 years.

Our positive finding for the association between TVviewing and BMI trajectory is concordant with some studies. In a longitudinal study of children followed from preschool to early adolescence (started in 1987), children who were in the highest tertile of TV viewing (≥3 versus <1.75 hours) had the greatest increases in mean BMI, triceps and sum of skinfolds from 4 to 11 years.[22] For each hour per day increase in TV viewing, there was a 0.09-unit increase in BMI among boys and girls in the 2004 to 2008 waves of the Growing Up Today Study.[148] Similarly, reducing TV viewing over one year was associated with lower BMI z-scores among adolescents in a secondary data analysis from an "obesity prevention" randomized intervention trial.[149] Given the multiple comparisons in the analyses, it is possible that our finding of a higher BMI trajectory from 4 to 12.8 years with ≥2 versus ≤0.5 hours of TV viewing/day is due to chance and requires replication.

The null association between TV viewing and anthropometry (weight trajectory and WC/waist-to-height ratio at follow-up) has previously been reported. In a population-based cohort of Australian adults (mean age = 48.3 ± 10.5 at baseline) followed from 2000 to 2012, those who increased (versus decreased) their TV viewing did not have significant increases in WC over a 12-year period.[63] Screen time was similarly not related to BMI in cross-sectional (age 10.8) and longitudinal analyses (ages 10.8-12.4) among children in three rural states in the United States.[57] In another cohort of children from Norway followed from 4 to 8 years of age, TV viewing was not associated with change in BMI Z-scores over time.[134]

Inconsistent findings reported across studies may arise from heterogeneity in the period of assessment of exposure and/or outcomes and length of follow-up; different measures of adiposity and tools used to measure them; incongruity in study designs and sample sizes; and diversity in population characteristics (e.g. ethnicity, socioeconomic status, lifestyle). The aforementioned null findings may be attributable to the characteristics of our study population. Most children in our sample were physically active and breastfed, had <2 hours of TV/day and had relatively low obesity rates compared with the United States population (1.1, 2.0 and 1.4% with Z-scores above 2 SD at 4, 10.8/11.8 and 12.8 years, respectively). However, with the steady rise in screen media and plunge in physical activity over the past two decades, these findings may be different if repeated in other populations today.

Consumption of unhealthy foods and snacks is a potential pathway through which TV viewing and higher BMI may be associated.[129] However, we were unable to directly assess the effect of diet as a mediator of the association between TV viewing and BMI because the foods did not represent a comprehensive list of the child's diet. We reported an increasing frequency of intake of unhealthy foods among those who watched ≥2 versus <2 hours of TV/day. This suggests that children who watch long hours of TV may eat unhealthy foods, but also that children who have unhealthy diets may engage in sedentary behavior, as dietary data was collected at the same ages as TV viewing.

Our findings should be interpreted within the context of the strengths and limitations of the study. Among the strengths, the study objectively measured height, weight and WC over time. The former two were measured at 3 points throughout life allowing us to assess the effect of TV viewing on change in BMI and weight Z-scores, while the latter allowed the examination of the relationship between TV viewing and WC and waist-to-height ratio Z-scores. Further, the study population is of a relatively homogenous ethnicity and socioeconomic status which reduced confounding by these variables, but limits generalizability of results.

The limitations of the study include potential recall bias of reported child's diet, TV viewing and physical activity by mothers approximately 6-9 years after the exposures. We were unable to assess the effect of other types of screen media on anthropometric measurements such as use of computers and video games. Missing these data may underestimate the true effect of screen-based sedentary behavior on trajectories. The limited range in physical activity reported by mothers reduced the opportunity to examine the joint effects of TV viewing and physical activity on trajectories over time.

CONCLUSIONS

Watching TV for $\geq$2 hours/day versus $\leq$0.5 hours/day was related to a higher BMI trajectory from childhood through adolescence, although this may be due to chance. TV viewing was not associated with weight trajectory from childhood through adolescence or Z-scores for WC and waist-to-height ratio in adolescence. Additional research is needed to assess the effect of measured sedentary behavior, including a variety of screen media, on growth trajectories, and the mediating role that diet may play in this relationship.

COMPLIANCE WITH ETHICAL STANDARDS

Conflict of Interest: The authors declare that they have no conflicts of interest.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

Chapter 5: Summary and Future Directions

SUMMARY

Obesity is a global epidemic with rates expected to rise dramatically by 2030.[65] This dissertation approaches obesity from a life course perspective, with a specific focus on early life exposures: age at SF introduction, and TV viewing and PA in childhood. We utilized linked mother-daughter dyads from the Nurses' Mothers' Cohort Study and the Nurses' Health Study II to examine the first two aims. We then utilized linked mother-offspring dyads from a nested case-control study of pre-eclamptic and normotensive pregnancies with offspring follow-up within a population-based cohort in Norway to examine the third aim.

Aim 1

The first aim assessed the association between age at SF introduction in infancy and obesity in childhood, late adolescence and adulthood. We hypothesized that both early (<3 months) and late (≥9 months) SF introduction, compared to introduction at 6-9 months, would be associated with higher odds of obesity across the life course. We report that introduction to SF at or after 9 months of age, versus 6-9 months, was marginally associated with odds of obesity at age 5, but not at ages 10, 18 or 25-42 years.

Aim 2

The objective of the second aim was to examine the impact of TV viewing in childhood on overweight and obesity throughout life, and to assess the joint effects of TV viewing and PA in childhood on overweight and obesity throughout life. The hypothesis was that those with ≥2 hours of TV viewing per day at 3-5 and 5-10 years, versus no TV viewing, would have higher risk of overweight and obesity at different stages of the life course, and that these effects would be considerably exacerbated when combined with low PA during the same period. Our findings suggest that 2 or more hours of TV viewing at 3-5 years, compared to no TV viewing, was associated with higher odds of overweight and obesity at ages 5 and 10. Four or more hours of TV viewing at 3-5 years, compared to no TV viewing, was also related to higher odds of overweight and obesity at age 18 and in adulthood. Similarly, ≥4 hours of TV/day at 5-10 years, versus no TV, was associated with higher odds of overweight and obesity at ages 10, 18 and in adulthood. The combination of low TV viewing/low PA, high TV viewing/high PA and high TV viewing/low PA at 3-5 and 5-10 years, compared to low TV viewing/high PA, were all associated with substantially higher odds of overweight and obesity across all age groups. The strongest observed effects appeared among those who did not meet both TV viewing and PA recommendations (i.e. high TV viewing/low PA). As such, there was a persistent signal from TV viewing alone, and in combination with low PA in childhood, on overweight and obesity across the life course.

Aim 3

The third aim was to examine the association between TV viewing in childhood and changes in BMI and weight Z-scores from childhood through adolescence and WC and waist-to-height ratio in adolescence. We hypothesized that children who watched ≥2 hours of TV/day at 3-6 years, versus ≤0.5 hours/day, would have the greatest increases in BMI and weight Z-scores from 4 to 12.8 years. We also hypothesized that TV viewing for ≥2 hours/day versus ≤0.5 hours/day at 3-6 years will be associated with higher waist circumference and waist-to-height ratio Z-scores at 10.8/11.8 and 12.8 years. We report that TV viewing for ≥2 hours/day versus ≤0.5 hours/day at 3-6 years was associated with a higher BMI Z-score from 4 to 12.8 years, but not change in weight Z-score over the same period, or waist circumference and waist-to-height ratio Z-score at 10.8/11.8 and 12.8 years.

CONCLUSIONS

Findings from this body of research add to the literature that suggests that early life exposures are important contributors to obesity, with specific effects often persisting into later life after adjustment for important confounders.

Chapter 2 addressed an important yet understudied aspect of infant feeding – i.e. age at SF introduction – and demonstrated that late age at introduction of SF (≥9 months versus 6-9 months) may be proximally associated with obesity, but that these effects do not persist beyond 5 years of age. These findings are in line with several studies which suggest that delayed SF introduction is linked with obesity in childhood.[34-36] We speculate that the effect of late age at SF introduction on obesity may be attributable to interactions between the prenatal and postnatal environment, changes in microbial diversity and composition, drivers of delayed SF introduction or the type of foods introduced to infants.

Further, studies suggest that the effects of age at SF introduction on obesity may differ by infant feeding status, with adverse effects seen among formula-fed infants.[37] However, my research did not reveal an association between age at SF introduction and obesity among formula-fed infants.

The birth years of the participants in our study (1946-1964) relate to the historical context of our results, with different infant feeding recommendations and available foods/diets during the birth years of the nurses than today. Statistics indicate that approximately 70% of infants were breastfed in the 1930s, but these levels waned to 50% in the 1940s, and by the 1950s and 1960s only 38% of infants were breastfed.[150] After the final dip in the 1970s, rates of breastfeeding began to rise again.[27,150] Similarly, trends in age at SF introduction shifted from one year of age in the 1920s to as early as two days of age in the 1940s-60s[27] to around 6 months today.[29] Nonetheless, these conclusions provide an important stepping stone for further research in recent birth cohorts and may be of public health significance for mothers and health care providers, given the current lack of adherence by mothers to infant feeding guidelines by the AAP.[30,151]

Chapter 3 turns to an exposure in early and late childhood – TV viewing – and reveals that this sedentary behavior, alone and in combination with low PA, is related to risk of obesity throughout life. These longitudinal associations are especially important, given that the seemingly saturated literature suggests that the cross-sectional associations are weak and inconsistent.[105] Moreover, the persistence of the signal from TV viewing independently and in combination with low PA on overweight and obesity in adulthood, even after adjustment for adult behaviors, suggests an important window for intervention for obesity early in the life course.

Posited mechanisms to explain the proximal and long-term associations between TV viewing and obesity primarily include decreased PA, increased consumption of unhealthy meals and snacks, and exposure to food advertisements. Other proposed pathways relate to poor sleep quality,[129] conditioning of food consumption in front of the TV, decreased metabolic rate, and distraction from memory formation, habitual food intake, and internal satiety and satisfaction cues.[122]

The aforementioned conclusions suggest that interventions need to address <u>both</u> screen time and PA in childhood as a means of preventing obesity across the life course. This is imperative given that meeting screen time guidelines alone or PA guidelines alone were still correlated with risk of obesity in childhood, adolescence and adulthood. Indeed, the prevalent lack of adherence to the AAP recommendations for screen time,[152] coupled with the known tracking of sedentary behaviors and biological outcomes from childhood to adulthood[49,50,153] makes this goal ever more crucial.

Chapter 4 builds on Chapter 3 by assessing the effect of TV viewing in childhood on change in BMI and weight Z-scores from 4 to 12.8 years and on waist circumference and waist-to-height ratio Z-scores at 10.8/11.8 and 12.8 years in a cohort from Stavanger, Norway. Findings from this aim suggest that two or more hours of TV viewing per day in early childhood versus half an hour or less per day may be associated with a higher BMI Z-score from childhood through adolescence, but not with weight Z-scores over the same period. TV viewing was unrelated to Z-scores for waist circumference and waist-to-height ratio in adolescence. In contrast to the method of outcome ascertainment from chapter 3, weight, height and waist circumference were measured objectively in this study, thus giving our findings further validity.

An important note to consider when interpreting our results is that this population was born in the nineties. Although this is a more recent birth cohort than the nurses studied in chapters 2 and 3, there are still important differences in the era of technology seen then and now. Handheld devices such as smartphones and electronic tablets were essentially non-existent in the 20th century, while desktop computers and video games were only just entering most households. Use of these forms of screen media is progressively growing today.[154]

Furthermore, in analyzing characteristics of the Norwegian children in our sample, it is evident that they are generally healthier than most populations studied in the United States today. For example, 86% of children in our sample had <2 hours of TV/day and 88% were active or highly active throughout childhood. At 10.8/11.8 years, the mean BMI and weight Z-scores were -0.13 ± 1.2 and -0.01 ± 1.1, respectively. Most children were breastfed for more than 6 months and their mothers had a normal BMI and adequate gestational weight gain.

The combination of the former two contexts begs the question: in a population with increasing screen time and access to different types of screen media, and in an environment with unhealthy food choices and physical inactivity, how will obesity rates and BMI trajectories be impacted? It is crucial that future research assesses the effect of the combination of these factors on anthropometric measures and body composition, and intervene to bring about behavior change and improve health of the population.

FUTURE DIRECTIONS

Age at Solid Food Introduction

Our work and others[34-36] demonstrated that late SF introduction (≥9 versus 6-9 months) may be associated with obesity in childhood. This effect did not however last beyond childhood. This research is in line with some but not all studies,[32,33] suggesting that there may be windows of vulnerability for SF introduction with adverse effects. Therefore, future work should re-assess the effect of age at SF introduction on obesity at different stages of the life course in different birth cohorts.

Next, the age at SF introduction-obesity relationship can also be assessed by infant feeding status. Data demonstrates that the negative effects of early SF introduction on obesity were only evident among formula fed infants.[37] Our research and others showed that SF introduction was not associated with obesity among formula-fed infants,[36] although we do report higher odds of obesity at age 5 and in adulthood among breastfed nurses who were introduced to SF at ≥9 versus 6-9 months. This set of findings may be due to chance or may indicate that adverse effects of early or late introduction on obesity may be acting through different pathways. Indeed, this is especially important to explore in current birth cohorts with different formula composition and rates and duration of breastfeeding than our cohort of nurses from the 1940s-60s.

Another important issue to address is the mechanism driving the association between late age at SF introduction and obesity, specifically pertaining to the microbiome. Research indicates that infants who are introduced to protein and fiber later are more likely to have lower microbial diversity and thus delayed healthy microbiota development.[86] However, further research is needed to confirm this association and to assess differences in infant microbiomes relative to age at SF introduction.

Obesity is a multifactorial condition that rarely results from exposure to a single experience. As such, future work on infant feeding practices might explore the effect of type of diet first introduced to infants, along with the effects of age at SF introduction. Trends in types of SF first introduced have been fairly consistent over the past three decades, whereby mothers have had the tendency to introduce cereals as an infant's first SF.[155,156] Nonetheless, the recommendations about the type and/or order of foods to introduce to infants are inconsistent and data on the implications of introducing different types of first foods are limited.

Recent research on the microbiome has demonstrated that the introduction of different dietary sources after weaning is associated with a change in microbial diversity. These exposures may ultimately predispose the infant to chronic diseases in adulthood, depending on the substrates readily available to bacteria in the gut. For example, with the introduction of complex carbohydrates to the diet, there is a shift in microbial composition with increased levels of Firmicutes, Bacteroidetes and Actinobacteria which are able to digest substrates beyond human milk oligosaccharides (HMO's).[157] A high intake of protein in the first two years of life has been associated with increased production of insulin-like growth factor 1, thus programming obesity in early life.[158] Moreover, research shows that development of a "sweet tooth" in infancy and/or early childhood may influence choice of foods consumed and body weight.[159] Consequently, early life diet may set the stage for eating habits and biological outcomes that last a lifetime. Given the altered microbial states in chronic diseases,[160] the association between diet and changes in gut microbiota[161] and the effect of diet on growth[158] and lifelong eating habits,[159] it is important to assess whether the type of SF first introduced to infants may influence future health.

Sedentary behaviors

Although we showed important effects of TV viewing in childhood on obesity that persists into later life, several questions remain unanswered. In this era of ever-expanding means of exposure to screen time,[162] future research should address the differential effect of exposure to a variety of modern screen media on obesity and whether the number of screens children are exposed to exacerbates such effects. Thus far, limited research suggests that TV viewing is more consistently associated with BMI than other types of screen time.[148] However, with the steadily increasing use of other forms of screen media,[163] this link may change over the next few years. Although the effects of prolonged screen time on obesity are likely to worsen, studies have also shown that active video games, such as "Dance Revolution" may provide a means for increasing PA concurrent to screen time use.[164] These research questions may shed light on the mechanisms underlying the association between screen time and obesity. If the persistent association between TV viewing and obesity is confirmed in future studies, it suggests that there is some aspect of TV viewing that impacts weight gain and obesity (e.g. higher amount of food advertising than is viewed on computers or video games), rather than or in addition to the act of sedentariness. In contrast, if evidence of higher PA with active video games and thus attenuated weight gain comes to light, this may indicate that it is the sedentary behavior that is strongly influencing the complex screen time-obesity relationship.

Along with the importance of type and frequency of screen time, upcoming studies may assess whether different programs accessed via screen media result in attenuated or higher odds of obesity. Studies demonstrate that exposure to violent entertainment may trigger problem behaviors such as antisocial behavior,[165] emotional distress[166] and poor sleep quality[167] – all of which have been associated with obesity.[168,169] It is possible that exposure to educational content or food advertisements related to healthy eating habits and PA may promote healthy behaviors.[170] Watching programs with limited food advertisements may also help to reduce obesity. Parental supervision of viewing material could limit access to programs with negative effects, encourage programs with evident benefits and ultimately predict lower BMI among children.[171]

Other proposals for future studies are to evaluate the effects of "time of the day" exposure. Thus far, research indicates that children watch more TV over the weekend and during the evening than during weekdays.[172] Both weekday[173] and weekend[60] TV viewing have been associated with obesity, but further research is needed to compare the differential effects of exposure to TV viewing timing of screen time throughout the day. It is plausible that watching TV closer to bedtime may impact sleep quality and thus obesity, but limited research has assessed this relationship. [174]

Similarly, upcoming work might explore whether having a TV in the bedroom is associated with higher odds of obesity. Children who have a TV in the bedroom watch approximately an extra hour of TV per day, have poorer dietary habits and consume less family meals,[123] and have shorter sleep durations[120,174] versus those without a TV in the bedroom. Consequently, research has demonstrated that children with a TV in the bedroom have higher odds of having excess BMI for age and sex and greater BMI gains from 2 to 4 years of age.[175]

Given that parents are consistently asked to limit their child's screen time, it is vital for researchers to also determine how screen time is being replaced – i.e. is PA increasing or are children participating in other sedentary activities as a result?[176] Another question to address pertains to the role of PA in negating the adverse effect of screen time on obesity. In other words, if screen time recommendations are not met but PA guidelines are met, does this reduce the negative influence of screen time on weight? Findings from our study and others[177] do not support this, but further research is needed.

Further research on pathways mediating the association between screen time and obesity are required. Thus far, several mechanisms have been hypothesized, but few studies have directly assessed their mediating effects on obesity (Figure 5.1).

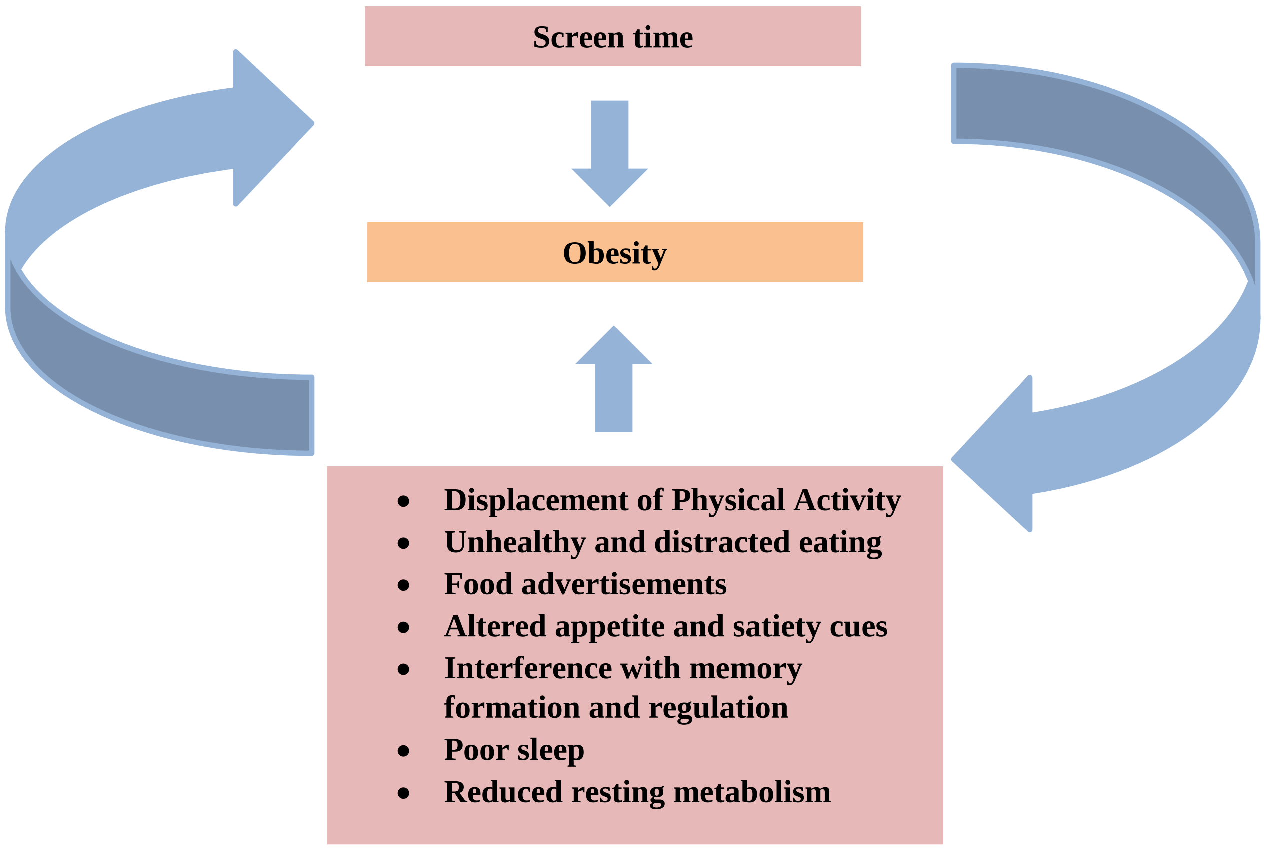

Figure 5.1 Posited Mechanisms Driving the Screen Time-Obesity Link

Lastly, as part of a life course epidemiology approach to obesity, it is important to attempt to pinpoint windows of vulnerability when high screen time and low PA may have their greatest effects on obesity, setting individuals down a dangerous, vicious cycle of unhealthy behaviors and outcomes. Answers to these queries may illuminate the importance of timing when screen time and PA may have their greatest effects on ill-health.

With regards to exposure and outcome ascertainment, it is essential that future research assess more objective measures of sedentary behavior (e.g. via use of accelerometers) and obesity (e.g. body fat). A systematic review of sedentary behavior in youth and obesity outcomes showed that, although there were mixed outcomes when self-reported screen time was examined in relation to incidence of obesity as measured by

BMI or waist circumference, most studies examining objectively measured screen time in relation to body fat did not detect such an association.[105]

Finally, additional studies are needed to examine changes in anthropometric trajectories from childhood into adolescence or adulthood, rather than incidence of obesity alone. This may help discern the individual effect of screen time on an individual's weight trajectory, rather than the rates of obesity within a population that may be attributable to many other factors. I hope to conduct some of this research as a postdoctoral fellow of the Cardiovascular Disease Epidemiology and Prevention T32 training program at the University of Minnesota.

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